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ORAL SMEARS IN THE DIAGNOSIS OF CARCINOMA AND PREMALIGNANT LESIONS

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THE cytologic topography and the physiologic variations of the oral mucosa of normal adults have been delineated by Montgomery[1] and by Ziskin and his associates.[2] Smears from healthy subjects consist almost exclusively of superficial squamous cells of cornified and noncornified types, with variable numbers of leukocytes and microorganisms. Except for increased numbers of cornified cells from the gingiva and palate and inconstant alterations in proportions of various types of superficial squamous cells during the menstrual cycle or during pregnancy, oral smears exhibit relatively constant patterns.[2-4]

Peters[5] noted more cellular smears and streaked or finely vacuolated cytoplasm and pleomorphism of epithelial cells in infections. He and others[3, 6] commented on the increased number of keratinized squamous cells in smears from patients with leukoplakia, lichen planus, and lupus erythematosus. He graded smears from leukoplakia into three categories according to the degree of atypism. Montgomery and von Haam[6] found that smears from the *uninvolved* mucosa in patients with leukoplakia also contained a high percentage of cornified cells.

Oral cytologic study has been recommended for the early diagnosis of carcinoma of the oral cavity and oropharynx,[5, 7-11] and cases have been reported in which malignant cells were found in smears from innocent-appearing lesions, such as granulation tissue, ulcers, bleeding points, and patches of leukoplakia, and from lesions which were not diagnosed by the initial biopsy. Silverman and his associates[11] used oral smears in the successful detection of four unsuspected cancers from sixty patients who had innocent-appearing ulcerated lesions of the mouth. Despite these provocative reports and the established reliability of

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exfoliative cytology in the diagnosis of early carcinoma of other mucous membranes, no studies relative to the accuracy of oral cytopathology in the diagnosis of *incipient* carcinoma of the oral cavity in large series of patients have been reported. However, there have been several reports attesting to the sensitivity of cytodiagnosis of *clinically evident* cancer of the mouth and oropharynx,[5, 9-13] with a sensitivity of from 86.7 per cent[12] to 95.8 per cent[5] and a mean accuracy of 94.5 per cent. The largest series was that reported by Peters,[5] who scored a creditable record of 193 positive and 59 suspicious smears from 263 carcinomas. The prediction of histologic grade of differentiation by examination of oral smears has been found to be reliable, provided that a sufficient number of cells are harvested in the smears.[14]

Recent reports have highlighted the value of oral smears in the detection of recurrent or residual carcinoma following treatment.[8-11, 14-17] The cytologic changes in irradiated benign and malignant cells from the oral cavity have also been documented,[5, 15, 16] and a preliminary investigation suggested a correlation between the intensity of such changes and prognosis,[15] but this was not confirmed in subsequent studies.[17]

The purpose of the present investigation was twofold: (1) to determine the accuracy of cytopathlogy in the diagnosis of untreated, residual, and recurrent carcinomas of the oral cavity and oropharynx, and (2) to investigate the potential diagnostic capabilities of oral smears in the differentiation of benign mucosal lesions from premalignant and early malignant conditions.

TABLE I. LOCATION OF CARCINOMAS IN FIRST SERIES

Tongue	26
Floor of mouth	17
Oropharynx	16
Gingiva	10
Palate	5
Tonsil	4
Lip	2
Total	80

MATERIAL AND METHOD

The first series consisted of eighty patients who had clinically evident carcinoma of the oral cavity or oropharynx (Table I). Smears were taken prior to treatment or during the first few days of roentgenotherapy. Additional smears were obtained from fifty-two of these patients at their monthly posttreatment follow-up visits. The second group was composed of forty-five patients who, during routine physical or dental examination, were found to have asymptomatic clinical oral leukoplakia.

TABLE II. ACCURACY OF CYTOLOGIC DIAGNOSIS OF EIGHTY CLINICALLY EVIDENT CARCINOMAS OF ORAL CAVITY OR OROPHARYNX

Positive	77 (96.3%)
Suspicious	0 (0.0%)
Negative	3 (3.7%)

The smears were obtained directly from the lesions by means of a moistened tongue blade. The material was spread evenly on glass slides, fixed immediately in 70 per cent alcohol, and stained according to the standard Papanicolaou technique.

The criteria of malignancy were those which have been applied to cytologic smears of other types of body secretions or fluids.

RESULTS

Cytologic Findings in Clinically Proved Invasive Carcinomas.—In the pretreatment smears, malignant cells were usually abundant (Fig. 1), although they seldom outnumbered the benign cells, and in some patients they were so sparse

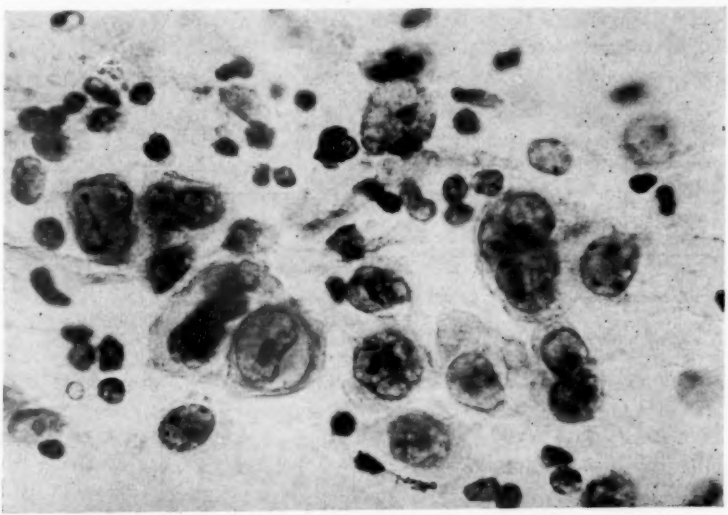


Fig. 1.—Direct smear from squamous-cell carcinoma of tongue. Note the pleomorphism, nucleocytoplasmic disproportion and the bizarre giant nucleoli. (Magnification, ×1280; reduced ⅓.)

that the smears had to be screened meticulously before any were detected. There was no constant relationship between the number of malignant cells and the size, location, gross features, or histologic degree of differentiation of the neoplasms. Invariably, the smears exhibited signs of inflammation (manifested by degenerative changes in the malignant and benign squamous cells and the presence of many leukocytes, variable numbers of erythrocytes, and mouth organisms).

Malignant cells were found in seventy-seven (96.3 per cent) of the eighty untreated carcinomas (Table II). Positive or suspicious smears were also obtained from twenty-one of twenty-three residual or recurrent neoplasms prior to biopsy confirmation and frequently before clinical suspicion was aroused

(Table III). In four patients, the positive cytologic findings were established *months* prior to clinical or histologic diagnosis. In these instances there were areas of granulation tissue, mucosal nodularities, or ulcers which persisted following treatment but were interpreted clinically as irradiation changes. One patient had positive smears over a period of nine months before pathologic examination confirmed the cytologic findings.

Generally, the smears from recurrent or residual neoplasms contained fewer malignant cells than did pretreatment smears. In fact, many of the positive posttreatment smears contained only two or three malignant cells, singly or in small clusters. This was especially true in cases in which there was no clinical suspicion of neoplasm. In view of the sparse populations in some specimens, it is not surprising that other smears from such cases were negative, thus accounting for the higher incidence of false negatives in this group. As shown in Table III, over 20 per cent of the *total* smears from residual or recurrent neoplasms were negative. In all but two instances this was compensated for by the examination of multiple specimens per patient.

TABLE III. ACCURACY OF CYTOLOGIC DIAGNOSIS OF TWENTY-THREE RESIDUAL OR RECURRENT CARCINOMAS OF ORAL CAVITY OR OROPHARYNX FOLLOWING X-RAY OR SURGICAL TREATMENT

	PATIENTS	TOTAL SMEARS
Positive	17 (73.9%)	31 (64.6%)
Suspicious	4 (17.4%)	7 (14.6%)
Negative	2 (8.7%)	10 (20.8%)

In most instances, the cytologic stigmas of inflammation were associated with the presence of malignant cells. The sudden appearance of pus cells in posttreatment smears from patients whose previous smears contained none indicated the appearance of recurrent neoplasm or the development of radionecrosis. On the other hand, atypical epithelial cells not associated with signs of inflammation were indicative of radiation-induced epithelial hyperplasia of the nonmalignant mucosa.

Irradiation occasionally caused sufficient epithelial atypism to pose interpretive difficulties (Fig. 2). Usually this was resolved by applying rigid criteria for malignancy or by assigning the smears to the "suspicious" category, but in two instances this led to false positive diagnosis (Fig. 2). In a study of this nature, an observer may be prone to assign greater malignant attributes to atypical cells than is warranted, thereby achieving increased but false sensitivity which results in a reduction of selectivity. Therefore, we directed attention to the cytologic findings in the patients who were clinically free of neoplasm following treatment to determine the magnitude of such overdiagnosis in this study.

TABLE IV. ACCURACY OF CYTOLOGIC DIAGNOSIS IN POSTTREATMENT FOLLOW-UP OF THIRTY-FOUR PATIENTS WITH NO RESIDUAL NEOPLASM

	PATIENTS	TOTAL SMEARS
Positive	2 (5.9%)	2 (1.4%)
Suspicious	2 (5.9%)	8 (5.6%)
Negative	30 (88.2%)	133 (93.0%)

Follow-up smears were available in thirty-four such cases (Table IV). All of the smears from thirty of these patients were negative; each of two patients had one false positive smear; and two others had a total of eight suspicious smears. Each of these overdiagnoses was the direct result of atypical hyperplastic cells masquerading as cancer cells (Fig. 2).

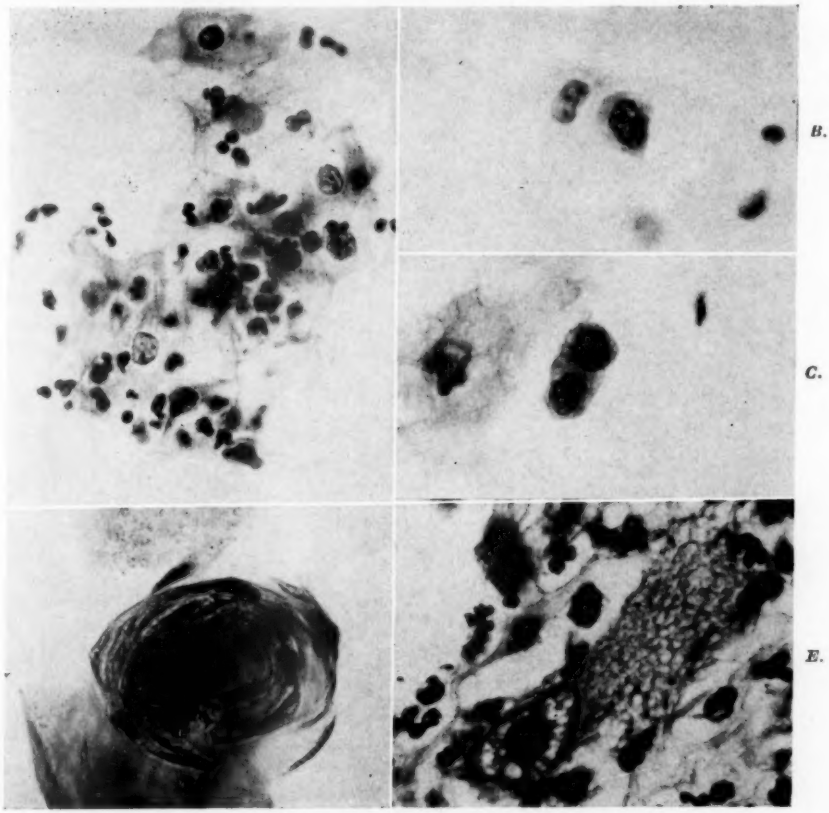


Fig. 2.—*A*, Direct smear from ulcerated area of radionecrosis. Note degenerating superficial squamous cells admixed with leukocytes. There is no epithelial atypism. (Magnification, ×860; reduced ⅓.)

B, Two atypical squamous cells. The one on the right may be mistaken for a malignant cell. (Magnification, ×1280; reduced ⅓.)

C, Bizarre nonmalignant squamous cells which led to false positive diagnosis (Magnification, ×1280; reduced ⅓.)

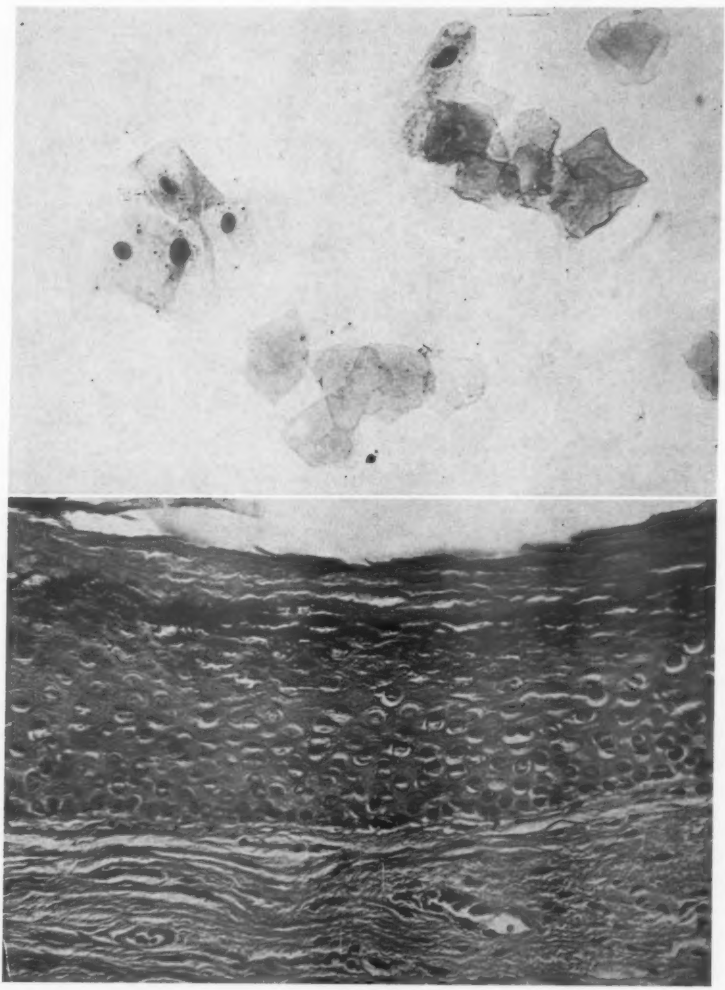
D, Large epithelial pearl composed of nonmalignant squamous cells. (Magnification, ×1280; reduced ⅓.)

E, Histologic section from same case. Bizarre giant cell in base of ulcer interpreted as nonmalignant cell of undetermined type by several pathologists. The nucleus in the lower left-hand corner represents all the features of malignancy. (Magnification, ×2560; reduced ⅓.)

Cytologic Diagnosis of Leukoplakia and Early Carcinoma.—Smears from white mucosal patches (Fig. 3, *B*) were characterized by many bright yellow, orange, or red superficial squamous cells; the nuclei were frequently pyknotic

or absent (Fig. 3, *A*). These cells represented keratotic scales, the opacity of which produced the white patches noted clinically. The smears from nine of the forty-five patients in this group showed, in addition to the evidence of hyperkeratosis, some nuclear atypism, enlargement, hyperchromasia, thickening and wrinkling of nuclear membranes, disturbance in the nucleocytoplasmic ratio, or abnormal nucleoli (Fig. 4). Histologic examination was performed

A.



B.

Fig. 3.—*A*, Direct smear from oral "white patch." Most of the cells have lost their nuclei and stain bright orange or yellow by the Papanicolaou stain, indicating advanced cornification. There is no atypism. (Magnification, ×410; reduced ⅓.)

B, Histologic section from same case showing mucosal hyperplasia with no atypism. Note distinct stratum granulosum beneath the cornified layer, so-called "epidermidization of mucous membrane." This is not true leukoplakia. (Magnification, ×410; reduced ⅓.)

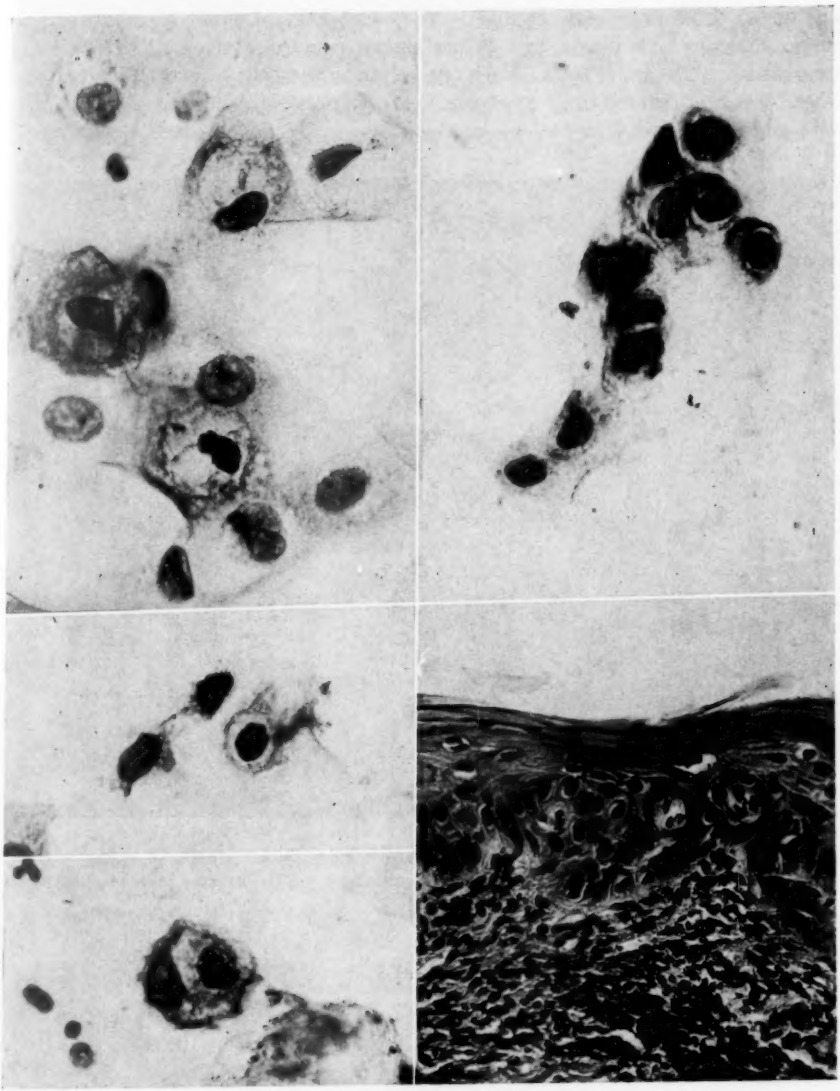


Fig. 4.—*A*, Direct smear from leukoplakia with early intraepithelial carcinoma. There are only mild alterations in the nuclei. Note abundant cytoplasm with many vacuoles. (Magnification, ×1280; reduced ⅓.)

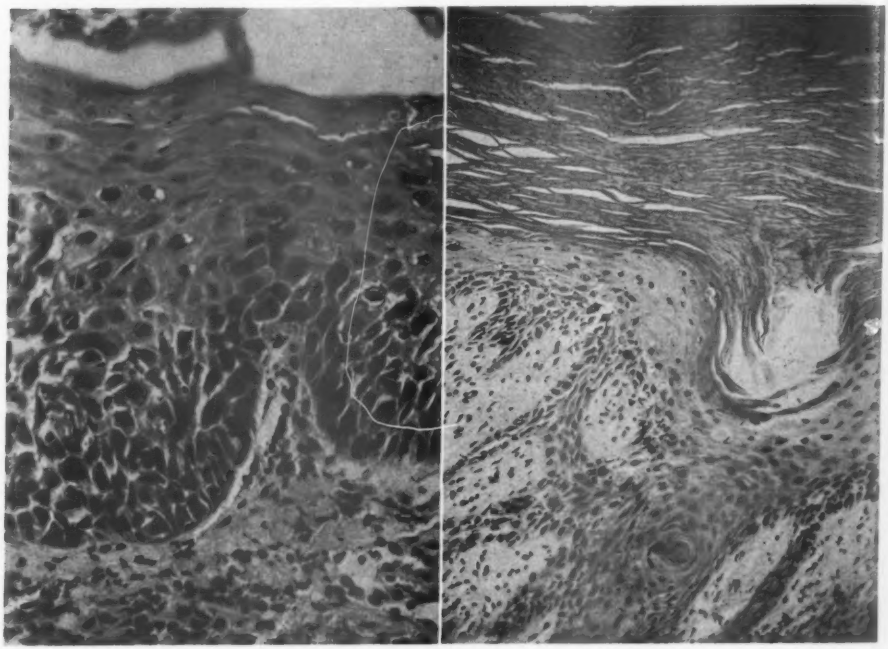
B, Strand of squamous cells showing nucleocytoplasmic disproportion and nuclear hyperchromasia. These were interpreted as suspicious for malignancy. (Magnification, ×1280; reduced ⅓.)

C, Three bizarre cells showing accentuation of the above features. (Magnification, ×1280; reduced ⅓.)

D, Binucleated atypical squamous cell. Note the increased and clumped chromatin. (Magnification, ×1280; reduced ⅓.)

E, Histologic section from same case. (Magnification, ×410; reduced ⅓.)

in four of these nine patients and in each instance exhibited significant pathologic change—leukoplakia in two and intraepithelial carcinoma in the other two (Table V). In contrast, only two of the thirty-six lesions from patients whose smears disclosed only hypercornification proved to be malignant or premalignant. In seventeen patients of this group no histologic studies were made.



A. *B.*

Fig. 5.—*A*, Histologic section from oral leukoplakia. The atypism is seen only in the lower layers. (Magnification, ×410; reduced ⅖.)

B, Histologic section from another case of oral leukoplakia. Note the thick keratotic scale covering the viable cells. Scrapings may consist only of these superficial cells, missing the atypical cells in the depths. (Magnification, ×210; reduced ⅖.)

There were two disturbing observations which may indicate obstacles to the cytodiagnosis of some of these lesions. The first was the frequent sparsity of atypical cells in smears from leukoplakia or leukoplakia with early malignant change. The other was the minor degree of atypism in other cases. Even when present, the atypism was seldom comparable in degree to that observed in vaginal or cervical smears from intraepithelial carcinoma of the cervix uteri. A review of the histologic preparations from these premalignant or early malignant oral lesions indicated that our fears were well founded (Fig. 5). Most of these lesions exhibited maximum nuclear abnormalities in the lower squamous layers; as the cells progressed upward, the nuclear atypism became less and less, resulting in superficial strata of epithelium in which the cells

showed little or no atypism (Fig. 5, *A*). In addition, the viable epithelium was usually covered by a thick scale of squamous-cell ghosts with pyknotic nuclei (parakeratosis) or with no nuclei (hyperkeratosis) (Fig. 5, *B*). Since most of the oral smears consisted principally of these outer cell "cadavers," it is not surprising that the cytologic findings sometimes did not mirror the severe alterations in the depths of the lesion.

TABLE V. CYTOLOGIC AND PATHOLOGIC CORRELATION IN FORTY-FIVE PATIENTS WITH CLINICAL LEUKOPLAKIA

PATHOLOGIC FINDINGS	CYTOLOGIC FINDINGS	
	NO ATYPISM	ATYPISM
Mucosal hyperplasia	17	0
Leukoplakia	1	2
Carcinoma in situ	1	2
Infiltrating cancer	0	0
No histologic examination	17	5
Total	36	9

DISCUSSION

The cytodiagnosis of clinically suspected oral cancer is accurate. However, since it gives no information concerning the presence or extent of invasion, it should not replace histologic examination. Its role in such lesions is a supporting one. Despite the lower accuracy of cytologic diagnosis of residual or recurrent carcinoma, the practical value of this technique in the follow-up of treated oral and oropharyngeal cancer is considerably greater, since repeated biopsies are not feasible; even if they were, it is doubtful that the precise biopsy site could be selected accurately, whereas oral smears permit the screening of the entire suspect area. This study, as well as those reported by others,[8-10] has shown that oral smears are capable of revealing therapeutic failures prior to the development of clinical evidence and are useful in distinguishing between residual healing reaction or radionecrosis and carcinoma. In this regard, certain cytologic interpretive difficulties have been encountered because of the cellular alterations induced by irradiation, difficulties similar to those encountered in the histologic diagnosis of similar tissues. We have commented on the sparsity of malignant cells in smears from residual neoplasms, due no doubt to the relatively small remaining surface area of cancer most of which may be submucosal. This indicates the need for examining more than one smear, especially when the warning cytologic signs of inflammation persist or develop. Fortunately, only a few residual or recurrent carcinomas are completely submucosal, a situation which precludes successful cytologic smear diagnosis.

It has been suggested only recently that oral cytology may be useful in the detection of early carcinoma or premalignant lesions in asymptomatic patients with innocent-appearing lesions, especially when they present as ulcers or granulation tissue.[5, 9-11] The cytologic diagnosis of the latter has a sound histologic basis, since the malignant cells have free egress and can be harvested by gentle abrasion. On the other hand, the atypical cells in leukoplakia are in the lower strata or are buried beneath thick mantles of keratinaceous debris

which comprises most of the material in scrapings from such lesions. Since leukoplakia is probably the most common premalignant oral disease, this is a serious obstacle to the successful application of this modality to early cancer detection. Although the findings in the present pilot study of clinical leukoplakia are encouraging, the failure to obtain cells from the deep layers of the squamous epithelium is disturbing and indicates the need for improved methods of abrasion. Our current efforts have been in this direction.

CONCLUSIONS

1. The oral smear diagnosis of eighty untreated carcinomas of the mouth and oropharynx was 96.3 per cent accurate.

2. Of twenty-three patients with residual or recurrent carcinoma following treatment, smears were positive in seventeen (73.9 per cent), suspicious in four (17.4 per cent), and negative in two (8.7 per cent) *prior* to histologic confirmation. Malignant cells were usually less abundant in smears from such neoplasms, and more than one smear was sometimes necessary to establish a cytologic diagnosis. In several cases a positive smear was the first indication of therapeutic failure and antedated clinical or histologic diagnosis by weeks or months.

3. The cytologic accuracy of posttreatment smears in thirty-four patients with no residual neoplasm was 93 per cent. In 133 such smears, there were two false positive (1.4 per cent) and eight suspicious reports (5.6 per cent).

4. Smears from each of forty-five asymptomatic patients with clinical leukoplakia revealed increased cornification. Nine of these patients also had smears which exhibited cellular atypism. Premalignant or early malignant changes were demonstrated in each of the four biopsied lesions in this group.

5. Oral cytology is an excellent adjunct to follow-up studies of treated oral cancers and may be an effective modality in the early detection of cancer and precancerous lesions of the mouth.

The photomicrographs were taken by Mr. George Hess, photographer, Veterans Administration Hospital, Ann Arbor, Michigan.

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OLFACTORY NEUROBLASTOMA (ESTHESIONEUROEPITHELIOMA) OF THE MAXILLARY SINUS

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THE olfactory neuroblastoma (esthesioneuroepithelioma) remains a rare entity in the medical and dental literature. However, Seaman[2] and Fruhling and Wild[1] present comprehensive studies of the existing literature. From 1924, when the tumor was first described by Louis Berger, to 1956 only twenty-seven neoplasms of a similar nature were reported. Most esthesioneuroepitheliomas fall into one of two categories—nasal gliomas and olfactory neuroblastomas. In the period between 1924 and 1951, eight olfactory neuroblastomas were reported in the French literature; none were reported by American or British authors, although Stout[3] observed six cases personally.

Since this tumor originates from the olfactory bulb, one would expect a greater reported incidence in the nose and associated structures of neoplasms that resemble those originating in the central nervous system. However, many of these tumors go beyond this stage and undergo sympathetic evolution, whereas others go unrecognized because of histologic confusion with glandular epitheliomas or sarcomas.[1]

Fruhling and Wild[1] report four cases in which olfactory neuroblastomas occurred in the nasal fossa, with one of these invading the maxillary sinus. In all, the symptoms were of a nonspecific nature, namely, nasal obstruction, head pain, and anosmia. The clinical picture made a differential diagnosis impossible. Only when biopsy specimens were examined histologically could a diagnosis be established, and even then selective and meticulous staining techniques had to be employed.

Seaman[2] lists eleven cases in patients ranging from 8 to 79 years of age. This group consisted of five male and six female patients. If any conclusions could be drawn from these cases, one would be that age and sex play no role in the development of these lesions. In one case there was metastasis to the cervical lymph nodes. Two of the eleven patients experienced recurrences after surgery and x-ray therapy. In eight cases, however, excellent results were obtained with surgical intervention followed by x-ray therapy.

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It is generally believed that, although not truly metastatic, these tumors are capable of invading neighboring bone structure. In the eleven cases listed by Seaman and the 4 described by Fruhling and Wild, the nasal fossa was the original site of the neoplasm.

CASE REPORT

J. B., a 24-year-old white man, entered the Providence Veterans Administration Hospital on April 15, 1956, with a chief complaint of pain and swelling of the left eye of three days' duration.

History of Present Illness.—Five days prior to admission, the patient seared his left eye with hot tar. Some tar remained in the eye but was removed by the patient's local physician. One month prior to admission, two upper left molars had been extracted, and the sockets had failed to heal properly. On the night that he was admitted to the hospital the patient complained of severe headache, slight disorientation, generalized malaise, a phase of toxicity, epistaxis, and hemoptysis.

The past history and system review were noncontributory.

Physical Examination.—On admission, the patient had a temperature of 101° F., and his blood pressure was 130/80. There was marked edema about both lids of the left eye. The pupil per se was not infected. There was some blood within the nares but no obvious bleeding point. Two unhealed necrotic sockets in communication with the antrum were obvious in the left maxilla. The entire left facial region was exquisitely tender.

Laboratory Findings.—The initial white blood count was 24,500 with a shift to the left. The hemoglobin was 14.2 grams. The urine showed a concentrated specimen with occasional white and red cells. Culture and sensitivity tests of the oroantral fistula taken on April 18, 1956, indicated the presence of alpha streptococcus which was highly sensitive to erythromycin. A white blood count on April 19, 1956, was 10,500 with a shift to the left.

Roentgenographic Findings.—On admission, the chest was normal. The right antrum was clear. There was complete opacification of the left antrum with what appeared to be a steel-wool-like shadow measuring 3.8 cm. in diameter (Fig. 1). A laminagram taken on April 17, 1956, showed a mottled calcific shadow, apparently within the left antrum.

In the postoperative roentgenogram taken on May 9, 1956, this shadow could no longer be seen. There was now complete opacification of the left antrum (Fig. 2).

Clinical Course.—The admission diagnosis was established as left maxillary sinusitis and oroantral fistula following extraction of two upper left molars. The patient was placed on hot saline mouth rinses and high doses of penicillin and streptomycin. The remaining involved teeth were extracted. The fistula into the sinus was curetted and packed with iodoform gauze. The patient was seen by the consulting ophthalmologist. His impression was that the patient had an orbital cellulitis secondary to a maxillary sinus and dental infection and that, therefore, the contents of the orbit were not in jeopardy. Upon receipt of sensitivity data from the culture of the oroantral fistula, penicillin and streptomycin were discontinued and erythromycin was substituted. The opening into the maxillary sinus was curetted and irrigated daily. On this regimen, the patient's initial temperature fell over a period of five days until he was afebrile. During this period he continued to cough up fairly large amounts of necrotic, pustular, bloody material. Eventually, he became ambulatory on the ward; he had no specific complaints, and the swelling in his orbital region was subsiding. A Caldwell-Luc operation on the left antrum, with repair of the left oroantral fistula, was recommended.

Report of the Operation.—May 8, 1956, gas, oxygen, and ether were administered by means of nasoendotracheal intubation. The patient was prepared and draped in the usual manner about the head and neck. The mucoperiosteum above the left canine fossa was

Fig. 1.—Preoperative roentgenogram, taken at time of patient's admission to the hospital, showing "steel wool" shadow in left antrum.

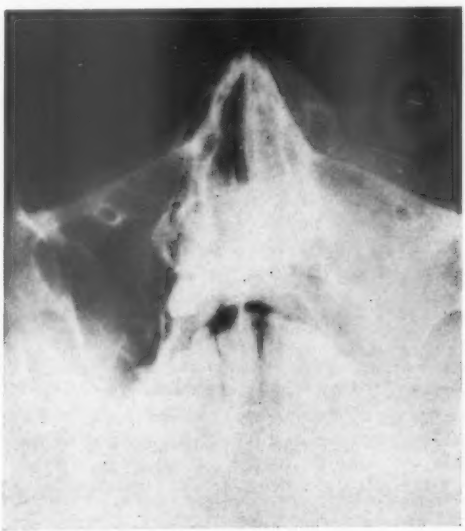

Fig. 2.—Postoperative roentgenogram taken on May 9, 1956.

incised and reflected, and the area was fenestrated with bone chisels and Kerrison forceps. The aperture was made large enough that the left maxillary sinus could be visualized adequately. The diseased membrane was curetted out in toto, and it appeared that numerous polypoid bodies were in the membrane. In addition, some calcified material was evacuated. A nasal trochar was then inserted into the left nostril, and the inferior turbinate bone was punctured to create an artificial ostium near the floor of the sinus for drainage. The sinus was packed with petrolatum gauze, the end of which protruded out of the left nostril. The wound in the canine fossa was closed with 000 Dermalon sutures.

The next procedure was the repair of the oroantral fistula. A curvilinear incision was made on the left side of the hard palate, and the mucoperiosteal tissues were reflected. The fistula was excised, and all granulation tissue was removed. On the buccal aspect of the aforementioned flap a small "V" of tissue was excised to permit a 90 degree rotation of the flap. The flap was then rotated over the oroantral opening and sutured into place with 000 Dermalon sutures. The bare donor area on the palate was packed with gauze soaked in tincture of benzoin. The operation completed, the patient was returned to the recovery room in good condition. His recovery was uneventful. The petrolatum gauze was removed on the sixth postoperative day, and the intraoral sutures were removed two days later. The patient was discharged on May 17, 1956, the tenth day after the operation.

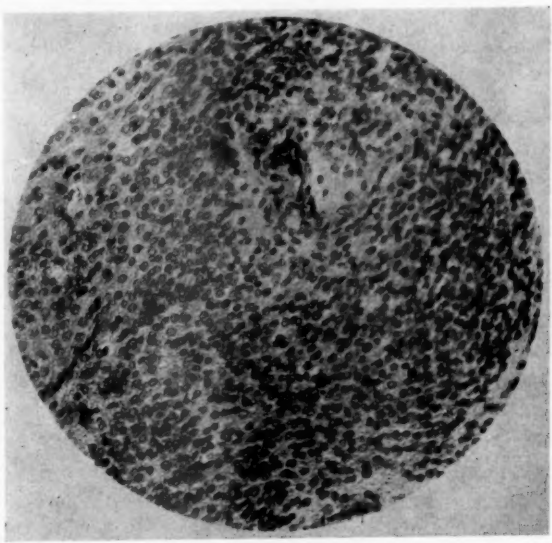

Fig. 3.—Photomicrograph of nasal mucosa containing closely packed cells in a neuroid stroma.

Microscopic Description.—Sections showed that the nasal mucosa contained infiltrates of rather closely packed cells with ill-defined pale red cytoplasm and regular, round, pale to dark nuclei with fine and sometimes coarsely stippled chromatin. These cells were in a fibrillar neuroid stroma. The stroma was very vascular, and many calcific concretions were dotted throughout. Special stains revealed that these monotonously regular, rounded cells were devoid of reticulum. Occasional mitotic figures were noted (Fig. 3).

Diagnosis: Neuroepithelioma of the maxillary sinus (esthesioneuroepithelioma).

Follow-Up.—The patient was seen one year later. He had no complaints or symptoms, and there was no evidence of recurrence.

SUMMARY

1. A case of olfactory neuroblastoma (esthesioneuroepithelioma) has been presented.

2. This tumor is quite rare; only twenty-seven cases have been reported in the world literature. It is usually located in the nasal fossa.

3. In the case presented here the neoplasm was confined to the left antrum, which is an unusual location.

4. From its radiographic appearance, it was thought to be an osteochondroma.

5. Symptoms are not specific, and therefore diagnosis is difficult. Proper diagnosis can be made solely by biopsy with special and meticulous histologic techniques.

6. Although these tumors are not metastatic, they are believed to be invasive in character.

7. They are amenable to treatment by surgical removal or, if there are recurrences, by surgery in conjunction with follow-up x-ray therapy.

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PATIENT'S REACTION TO CHAIRSIDE ORAL SURGICAL TEACHING

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THERE have been few attempts to evalute the patient's reaction to chairside oral surgical teaching, even though chairside instruction is a well-established method in the teaching of dental students and graduate oral surgery students.

Much has been written and said about the patient-dentist relationship. Many textbooks, articles and essays have pointed out the importance of tact and good chairside manners, but all of these have been primarily appeals for a sympathetic consideration of the patient and have not been based on studies demonstrating the effects that chairside teaching may have upon the patient.

CHAIRSIDE TEACHING METHODS

Chairside teaching at the Research and Educational Hospital Oral Surgery Clinic, as at most teaching hospitals, consists of the presentation of the history and physical examination by the student or intern, the examination of the patient by the attending man, and a discussion of the case. Usually the attending man, the oral surgery staff, and two students go straight to the chairside of the patient who is to be presented. Some attending men prefer the presentation in the conference room without the patient's participation; others prefer the entire teaching procedure at the chairside; and others begin the discussion at the chairside and complete it in the conference room.

In the group there may be as many as five to ten, and sometimes more at the chairside. The student or intern to whom the case has been assigned describes the history and physical findings and presents the x-ray and laboratory data. The patient is then examined by the attending man and occasionally questioned. If physical findings are found noteworthy, the staff is invited to re-examine the patient. Discussion often begins during the examination. The attending man may ask the group for comments, or he may question the interns or residents on a differential diagnosis. Frequently, he talks about similar cases from his own experience and focuses attention on disease entities in general rather than on the specific patient or his illness.

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The chairside presentations may consist of only a single case or several cases. These may last from a few minutes to thirty minutes or longer, depending on how well the case is known to the group, how interesting the patient is for teaching purposes, or how bizarre the case may be.

The atmosphere in which the chairside teachings are conducted is a friendly one. Usually, the intern or resident introduces the attending man to the patient. Staff and students feel free to ask questions and express opinions, even though they differ from those of the attending man. On most case presentations discussions are encouraged and often animated on the blackboard. At times, when a patient with an incurable condition is discussed, some member of the group reminds others to move out of hearing. Often, however, patients are still able to hear the discussion.

EXPLORATION OF PATIENT'S REACTIONS

In order to find out what the patient's reaction to this chairside teaching is, we decided to make observations of changes in facial expression, pallor, blushing, perspiration, agitation, crying, smiling, resentment, apprehension, etc. during the presentations. Note was taken when these changes occurred as the group approached the chair or during the presentation, examination, and discussion. At times important features of the discussion were noted. Facetious or ambiguous remarks and medical or dental terms that were considered traumatizing to the patient were also noted. Pulse, respirations, and blood pressure were sometimes noted during the presentation and discussion.

Patients' reactions were explored by interview immediately after termination of the discussion. The interval of time between the presentation and the end of the discussion varied from one minute to several minutes, the longest being one-half hour. The interviewer was always recognized by the patient as a member of the chairside group. We started the interview by some such question as, "How do you feel seeing so many doctors around you discussing your problem?" Comments were invited regarding various remarks and terms used during the presentation and anything specific. We also tried to find out how much the patient understood about the terms, abbreviations, etc. that were used. In addition, attention was directed to staff members, their way of conducting the presentation, examination, discussion, and teaching; certain mannerisms and reassuring attitudes were also noted.

A few attending men, staff, and students were questioned about their attitude toward chairside teaching and were invited to comment freely.

CASES

One hundred thirty-two patients were interviewed at the chairside over a period of six months. Their ages ranged from 16 to 73. Sixty-eight patients were males. All 132 were presented, discussed, and interviewed concerning their reaction to the teaching procedure. Ninety-two patients were presented and discussed at the chairside; twenty-three patients were presented at the chairside, but the discussion took place in the conference room; seventeen cases were

discussed in the presence of the patient after the student had made the presentation, and findings were discussed in the conference room without the patient's being present.

Most of the patients were examined during the teaching session by the attending man or by group members.

REACTION TO CASE PRESENTATION

Only a few patients showed a mild or marked apprehensive reaction during the case presentation.

One patient was very alert for any inaccuracies in the historical data presented by the intern and took pride in the corrections. However, when the intern reported information that he had received from the patient's previous oral surgeon and that the patient had not revealed (namely, that he had been addicted to a drug) the patient was not only surprised but resentful at having the truth brought out in front of the group.

Another patient was angry when her marital separation was mentioned in connection with her facial swelling. She felt humiliated and could not understand what her private life had to do with her present condition. She regretted having discussed her private life and said that she would not have done so had she known that it would be discussed in general.

Another patient is worth mentioning because she demonstrated that not only what is said but how it is said is important. A resident presented the case of a 52-year-old woman with a submaxillary mass, carefully avoiding expressions that could give a hint to the woman who had a cancerophobia. As he described the mass under the mandible, however, the tone of his voice slightly changed. This made the patient suspicious and convinced her that her life was endangered.

An obese female patient was to be presented to students in the clinic. She was not informed about the plan and thought she was to have x-rays. When she suddenly found herself in the middle of a large group, she was "frightened." During the history she was confused and hardly able to answer questions. Later she said she felt ashamed in front of a large group.

The great majority of patients expressed satisfaction with the presentation and said that they enjoyed the attention received and the chance to ask questions. Twelve patients said that they were disappointed, as they would have liked to hear more; five others were indifferent. Three patients expressed concern and became convinced that something more was wrong since the discussion was withheld from them.

REACTION TO CHAIRSIDE DISCUSSION

The discussion of ninety-two cases took place at the chairside.

In the majority of cases the physical findings were presented first, and most of the patients expressed complete satisfaction concerning the discussion. Others were pleased that so much time was spent on them. Several patients remarked favorably on the attending man's reassuring words. One man said

it made him feel important to have his name mentioned. Still another male patient stated that he was helped just by listening, and several female patients said that they felt better.

Only a few patients expressed open resentment against the procedure of chairside teaching. One man being treated for an osteomyelitis thought that he was treated like a guinea pig, and another became angry because some of his questions were seemingly ignored by the group around him.

Thirty-three patients claimed to have followed the discussion with understanding and knowledge of the terms. In later questioning eighteen gave evidence of their understanding. These patients had known illnesses and had been hospitalized previously. Most of the terminology was not only unfamiliar but also misunderstood and misinterpreted by the patients. It appears that the greater the patient's fear about his condition, the more vulnerable he seems to be toward distortion, misunderstanding, and confusion.

Several patients expressed concern over the different opinions expressed by the group.

Many stated that "they were left in the dark." They wanted a clear explanation. Some patients got the impression that the doctors were uncertain. Most patients were even more concerned about the prognosis than about explanations.

A few patients openly expressed their opinion that the chairside discussion was initially for teaching purposes.

DISCUSSION

Most patients presenting for oral surgical treatment also have a great deal of anxiety and often fear. Whether expressed or not, the fear of pain, suffering, and sometimes death is always present. With this in mind, to help diminish the emotional impact of the chairside presentation on the patient, we believe that it is important to know the amount of apprehension and fear that the patient already has in relation to his condition. This should be evaluated, and if there is too much apprehension the chairside presentation should be kept to a minimum.

Chairside presentations and discussions should be conducted with a constant awareness of the patient's feelings. Every effort should be made not to embarrass, frighten, or irritate the patient. Intimate secrets of the patient that is pertinent to the case should not be mentioned in his presence. Threatening terms and phrases should not be used during the patient's interview when other terms are always available. "Acid-fast condition," "lues," "Neisserian involvement," "decompensation," "Bard-Parker approach," "Caldwell-Luc opening," and many other terms have spared many a sensitive patient. The attending man, as well as the teaching group, must avoid showing doubt, uncertainty, or pessimism in association with the case, not only in what is said but in the manner of saying it. Brief, simple, and reassuring explanations should be made whenever possible during the conduct of the chairside presentation, and the patient's questions should always be answered. The patient can always be made

cheerful by telling him that he can expect to be more comfortable soon. The frequent use of the patient's name can be very helpful. Nothing can be more effective in removing anxiety as the sound of the patient's own name.

The patient should be told the results of the conference as soon as possible, with tact, kindness, and diplomacy. A few kind words from the attending man often mean a great deal to the anxiously waiting patient and are of great reassuring value to him.

CONCLUSION

Even though chairside teaching is a well-established procedure in the education of dental students and graduate oral surgery students, there have been few attempts to evaluate it in terms of its effect upon the patient. In this study, 132 patients were interviewed at the chairside before, during, and after case presentations and discussions.

The majority of patients expressed satisfaction with the presentation and discussion, and these teaching exercises were often greatly reassuring to the patient. Only a few patients showed a mild or marked apprehension reaction during these teaching exercises.

Certain suggestions from the patient's viewpoint, gained on the basis of this study, are as follows:

1. The patient should be prepared for chairside teaching if his emotional attitude is unstable.

2. He should be portected from disturbing statements during the interview.

3. Chairside presentations should be conducted with constant awareness of the patient's feelings and recognition of the importance of the "whole patient."

4. After a case presentation, a conference should follow in a conference room.

5. The patient should be told the results of the conference as soon as possible, so that he may ask questions and receive adequate reassuring explanations.

EXODONTIA

THE DELAYED TREATMENT OF UNERUPTED TEETH IN THE EDENTULOUS MOUTH

Report of a Case

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THE importance and value of the dental roentgenogram are well established. Nevertheless, this basic tool of dental practice is often overlooked in the diagnostic and treatment-planning procedures when an edentulous patient presents himself for the first time. Adequate roentgenograms may reveal unerupted teeth whose presence has been hitherto unsuspected by the patient. Should these teeth be removed or allowed to remain? As a general rule, we feel that they should be removed.

However, when unerupted teeth lie in close proximity to vital structures or present problems which make their removal a difficult surgical procedure, the dentist must consider carefully before recommending either removal or retention. Maxillary teeth may encroach upon the maxillary sinus, the floor of the orbit, or the nasal cavity. Mandibular teeth may lie near the mandibular canal or near the inferior border in such a position that they can be reached only from an extraoral approach. A thorough examination of the roentgenograms may show that the follicular space, which normally decreases in size as the enamel organ atrophies with age, is almost or entirely absent, and this is another condition which complicates surgical removal. In many cases, there is reason to suspect that actual union between the tooth and the bone has occurred, obliterating the periodontal membrane space. This union, which is usually referred to as an ankylosis of the tooth to the bone, may require that the tooth be literally fractured from its bed.

The presence of a cyst around an unerupted tooth may appear to complicate removal of that tooth, but frequently it simplifies the problem. The space

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created by the cyst usually provides easy access to the tooth by decreasing the amount of bone that must be removed surgically.

In many cases, the tooth may appear roentgenographically to be innocuous. Many such teeth remain quiescent throughout the patient's life. These are the teeth that may be retained. A word of caution is in order, however, concerning those cases in which severe alveolar atrophy may occur, with the mandible resorbing to the point where the diameter of the bone is little greater than the diameter of the tooth. The tooth disrupts the continuity of an already weakened bone and a pathologic fracture may occur. If this condition can be anticipated, the tooth should be removed before the danger point is reached.

Before recommending retention, the dentist should (1) inform the patient of the condition, (2) explain the surgical problems involved, (3) warn the patient that subsequent changes may require that the tooth be removed, and (4) make certain that the condition will be followed by adequate periodic examination. Before recommending removal, the dentist must be sure that the surgical procedure will not leave the patient with a problem more serious than that with which he presented.

The case that follows is that of a patient who was told to disregard her unerupted teeth until they caused some difficulty. Fortunately, since she had a series of roentgenograms going back to the time her erupted teeth were removed, we were able to follow the sequence of events leading up to the present chief complaint.

CASE REPORT

A well-developed, well-nourished, 39-year-old Negro woman came to the Oral Surgery Department of Northwestern University Dental School on the afternoon of Aug. 5, 1959, with the chief complaint of a swelling of the left side of her face.

Onset and Course.—The swelling had been present for approximately one month, with intermittent periods of enlargement and remission. The patient attributed this to the air-conditioning system in the restaurant where she worked. A similar swelling had also occurred approximately two years previously but had subsided without treatment.

About six years ago, the patient began to notice loosening of her teeth, and her gingivae were painful. She went to her dentist, who took full-mouth roentgenograms and a left lateral jaw roentgenogram (Fig. 1). He told the patient that she had impacted upper and lower left third molars and that the lower third molar was situated high in the ascending ramus of the mandible. He explained the problems involved in their removal and advised that they be retained unless they began to give her some difficulty. The remaining erupted teeth were removed and dentures were constructed.

In June, 1958, the patient was referred by her dentist to a radiologist for a checkup of the left jaw. The radiologist's report, given to the patient with the film, stated: "Radiographic examination reveals no definite evidence of any bone injury. There is an impacted lower posterior molar tooth present on the left side." (Fig. 2.) Our examination of this film revealed a 2 cm. radiolucency surrounding the crown of a mesioangularly positioned molar in the ascending ramus of the left mandible. Comparison with the film taken five years earlier (Fig. 1) showed that this radiolucency had increased in size.

Past Medical History.—The past medical history revealed no disease which might have caused the swelling. There was no contraindication to surgery.

Physical Examination.—The patient was a well-developed, well-nourished, very cooperative Negro woman in no acute distress.

Extraoral examination revealed a 5 by 8 cm. swelling over the left parotid and masseteric region. It was firm, warm, and tender to palpation. There was moderate trismus.

Intraoral examination revealed an edentulous mouth in apparent good health except in the lower left third molar region, where the opening of a sinus tract, 3 mm. in diameter, was present on the buccal aspect near the crest of the ridge. Pressure on the anterior border of the ramus produced a seropurulent exudate from the opening and elicited a painful response from the patient. In the upper left third molar area an elevation on the buccal surface of the ridge could be palpated. This was assumed to be the upper left third molar. There were no clinical signs of infection or pain in this maxillary area.

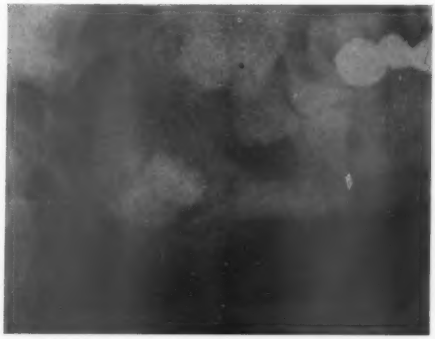

Fig. 1.—Lateral view of the left mandibular ramus in 1953.

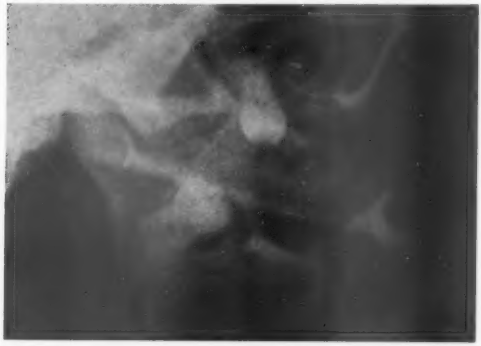

Fig. 2.—Lateral view of the left mandibular ramus in 1958.

Roentgenographic Examination.—Intraoral films of the left ascending ramus revealed the crown of a molar tooth, surrounded by a radiolucent area which appeared to have eroded through the anterior border of the ramus. A study of the extraoral films which the patient presented (Figs. 1 and 2) showed that the tooth lay in a mesioangular position approximately halfway between the inferior border and the tip of the coronoid process of the mandible. In both films the crown was surrounded by a radiolucency, but an increase in size was apparent in the later film.

Preoperative diagnosis: Cyst, follicular, involving a retained lower left third molar located in the ascending ramus.

Treatment.—On Aug. 5, 1959, the sinus tract was irrigated with warm normal saline solution followed by hydrogen peroxide (1.5 per cent) through a blunted 15 gauge needle on a 10 c.c. Luer-Lok syringe. Procaine pencillin, 600,000 units, was administered intramuscularly. The patient was instructed to use warm saline lavage every hour for the remainder of the day and to return the next morning for surgical removal of the tooth and the cyst.

On the following morning she was given ¼ grain of butabarbital sodium (Butisol sodium) orally and another 600,000 units of procaine penicillin intramuscularly. Local anesthesia was obtained with an inferior alveolar nerve block, a long buccal injection, and infiltration into the soft tissue lateral to the ascending ramus. It was noted that seropurulent matter was extruded from the sinus tract during the long buccal injection. When the anesthetic had taken effect, an incision was made along the external oblique ridge and up the lateral edge of the anterior border of the ramus for a distance of approximately 2 cm. Reflection of the mucoperiosteal flap laterally exposed the anterior border of the ramus, which was partially resorbed. The bucco-occlusal aspect of the tooth could be seen. It was surrounded by a cystic lining and granulation tissue. In order to expose the tooth and allow for its delivery, we drilled a series of holes, 3 mm. apart, through the buccal bone with a bibevel burr pointing toward the bifurcation of the roots. These holes were connected with a cross-cut fissure burr in order that the collar of restricting bone might be removed in one segment with rongeur forceps. The tooth was luxated with a Potts elevator and delivered with an upper bicuspid forceps. The buccal ledge of bone was filed smooth. The cavity was irrigated and curetted, and Gelfoam was packed against the bleeding points in the apical area near the mandibular canal. The incision was closed with six interrupted 000 black silk sutures. Iodoform gauze was inserted as a drain. An external pressure dressing was applied to the left parotid and masseteric region. Empirin Compound was prescribed for relief of postoperative discomfort. The patient was instructed to relax for the remainder of the day, to use warm saline mouthwashes hourly, and to apply a hot-water bottle to the swollen area. She was restricted to a soft, liquid diet. She was dismissed and asked to return the next day. The tissue that had been removed was sent to an oral pathologist for microscopic study.

On the first postoperative day some swelling was present, both extra- and intraorally. The pressure dressing and drain were removed, 600,000 units of procaine penicillin was administered intramuscularly, and the patient was asked to return three days later.

On the fourth postoperative day the patient returned in good spirits, stating that she had been comfortable over the week end. The extraoral swelling was now more diffuse but had decreased in size. The sutures were removed, and a postoperative lateral jaw film showed an irregular faint radiolucency in the area from which the tooth and cyst had been removed (Fig. 3).

On the sixth postoperative day the swelling had almost completely resolved. The area was irrigated intraorally with normal saline solution. The patient was asked to return in one month.

Thirty days after the operation the patient stated that she felt that there was a slight swelling at the inferior border of the left mandible and that the operated area in her mouth was slightly sensitive. The swelling was not apparent to the examiners, and the patient was referred for adjustment of her lower denture which was irritating the healed mucous membrane in the left molar area.

Eighty-eight days after operation the patient returned to the clinic for removal of the retained maxillary left third molar. Examination revealed that the site of the previous surgery was well healed. At this time, a postoperative left lateral jaw film was taken, revealing normal osteogenic activity. The maxillary impaction was removed. When this area had healed the patient was referred for new dentures.

Histopathology.—Examination of the cyst membrane revealed that the stroma consisted of highly vascular fibrous connective tissue, with many thick- and thin-walled vascular spaces. It was heavily infiltrated with chronic and subacute inflammatory cells, chiefly lymphocytes,

polymorphonuclear leukocytes, and plasma cells. Also found in the stroma were numerous extravasated erythrocytes, cellular debris, blood pigment, occasional spicules of calcified material, and Russell's bodies.

The lumen was lined with a narrow layer of slightly hyperplastic stratified squamous epithelium, which was undergoing some vacuolar degeneration. It was heavily invaded with inflammatory cells. No sign of ameloblastoma was seen. The final diagnosis was cyst of the follicular type.

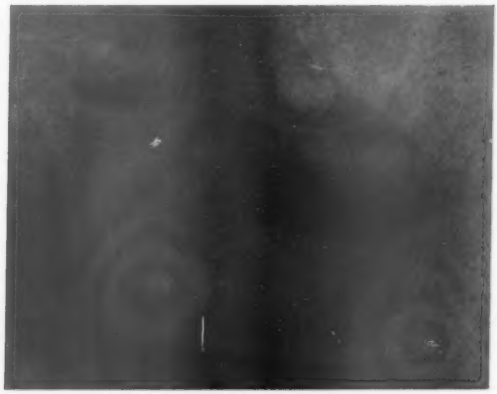

Fig. 3.—Lateral view of left mandibular ramus in 1959, four days after operation.

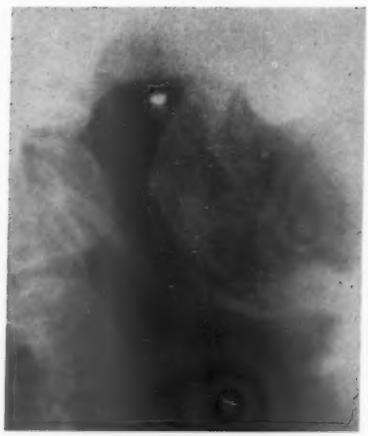

Fig. 4.—Lateral view of left mandibular ramus eighty-eight days after operation.

SUMMARY AND CONCLUSION

A case illustrating the delayed treatment of a retained mandibular third molar has been presented. We feel that a delay was justified in this case, since (1) the patient was told of the condition and warned that a situation might arise in which the tooth would have to be removed; (2) the surgical procedure

involved, when weighed against the possibility that the condition might remain asymptomatic, favored retention; (3) follow-up care was planned and carried through. The development of a follicular cyst and its extension into the soft tissues, with subsequent infection, led to our decision to remove the tooth and the cyst. Delayed treatment is indicated only when early treatment may do more harm than good.

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ORAL MEDICINE

FAMILIAL INTESTINAL POLYPOSIS WITH MELANOSIS ORIS: THE SYNDROME OF PEUTZ AND JEGHERS

Report of a Case

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WHEN attention is directed to what, in a sense, is a "medical curiosity," there often is a tendency for the rarity suddenly to become somewhat more common. This is precisely what has occurred in the last ten years with respect to a rather unusual group of symptoms known as the Peutz-Jeghers syndrome.

The syndrome of familial gastrointestinal polyposis with mucocutaneous pigmentation (melanosis oris) can hardly be considered a common disease now; nevertheless, more than 100 case reports have appeared in the medical literature in recent years. It is probable that many more cases remain unreported.

To Johannes Peutz,[52] a Dutch physician, must go the credit for first reporting this remarkable disease in 1921. Studying three generations in one family, Peutz noted an unusual distribution of melanin spots on the oral tissues and on the skin of the hands and feet of nine out of the twenty persons in the family. Further study showed that seven of the nine affected members demonstrated intestinal polyps.

Interest in the disease lay relatively dormant until 1949, when Jeghers, McKusick, and Katz[41] published their dynamic account of ten cases of this condition. In a careful review of the literature, they noted that in 1896 Sir Jonathan Hutchinson[39] observed, in a pair of 12-year-old twin girls, "a number of black pigmented spots on the lips and the inside of the mouth." A previous short report by Conner[18] on the same pair of twins revealed that the girls were dark complexioned and anemic. In 1919, Weber[78] reported a follow-up study on Hutchinson's cases. He stated that one of the twins had died at the age of 20 years as a result of intussusception. The other was reportedly in good health

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at the age of 35. (Jeghers and colleagues postulate that the intussusception could possibly have been the result of intestinal polyposis.) Weber also noted no pigmentation in other members of the twins' family.

In 1902 Sir Humphrey Rolleston[60] described the case of a 40-year-old man who suffered from abdominal pain, constipation, and tenderness of the right lower abdomen. Peculiar vertical black lines were noted on the lower lip, but Rolleston neglected to correlate these with the intestinal symptoms. Van Dijk and Oudendal,[74] in a paper entitled "Adenoma of Small Intestine With Contribution to Knowledge of Heredity of Tumors," contributed two more cases—those of a 16-year-old Indonesian-European boy and his 25-year-old sister. Both of these patients suffered from repeated colicky attacks and, on laparotomy, were shown to have adenomas. The typical orofacial pigment was present in both patients.

Almost twenty years later Foster[30] reported the cases of a father and daughter who presented themselves with intussusception which, on laparotomy, was found to be due to intestinal polyps. These patients also demonstrated a "diffuse brownish pigment of the lips and face." Further investigation of the father's family revealed similar symptoms in the father's brother and possibly in another relative. The latter was admitted to the hospital with what was considered a possible case of Addison's disease.

Touraine and Couder,[70] in the French literature, contributed another possible case. The pigmentary lesions were typical, and the patient had occasional rectal prolapses. A mobile polyp extending from the anus was shown on biopsy to be a simple adenoma. In another article published the following year,[69] the same authors collected from the literature thirty-one cases with a pigment pattern similar to that seen in the cases of Peutz and in their own previous case. "Peri-orificielle" was the French term that they used to describe the typical pigmentation. Twenty-two of the cases were familial, and in three of the cases the history suggested the possibility of polyps. Nevertheless, none of the thirty-one patients had been examined for gastrointestinal lesions.

The diagnosis of the Peutz-Jeghers syndrome can be made on the basis of three major symptoms: (1) a distinctive distribution of pigmentation of the oral mucosa and lips (melanoplakia); (2) gastrointestinal polyps, particularly of the small intestine; and (3) the hereditary or familial nature of the disease.

PIGMENTATION

Pigmentation, by virtue of its nature and distribution, appears to be the most essential and unique aspect of the disease. It is this feature that is of primary interest to the dental profession.

The pigment almost always occurs on the lips (particularly the lower lip) and the buccal mucosa. The hard palate, tongue, gingiva, floor of the mouth, and soft palate are less commonly affected. Extraoral pigmentation is most common on the face, although it occurs also on the hands and feet. Jeghers refers to the mouth pigmentation as being the "sine qua non" of the syndrome.

The pigment spots, which are described as macules varying in color from light brown to dark brown to blue-black, are 1 to 5 mm. in diameter. The skin

spots are usually dark brown, whereas the oral pigmentation is more black in tone. More often than not, the spots occur in groups of from two or three to several hundred. It is not uncommon, however, to see single spots. The macules demonstrate clearly defined margins and occur in close proximity to each other. They have little tendency to coalesce. They are level with the mucous membrane or skin. They are not hairy, nonvascular, and nonirritating, and their distribution or number bears no relationship to the number or severity of the gastrointestinal lesions. When examined with a high-power magnifying glass, some of the spots show a stippled appearance.

The cutaneous pigmentation is usually located in the area of the facial orifices. The spots are most commonly seen on the skin around the mouth, eyes, and nostrils. The limbs, including the palms of the hands and the soles of the feet, are less frequently affected.

The pigment is said to be present at birth or to occur during early childhood, but there are cases on record in which both the oral and the cutaneous components appeared late in life. Troxell's[72] patient first noted the pigment at the age of 75, and the patient described in this article did not show the pigmentary pattern until he was 68 years old. Many investigators have observed that the facial pigment has a tendency to fade, beginning in the third decade of life. The mucosal portion of the syndrome, however, appears to persist.

Both Peutz and Jeghers were aware that all of their patients were either dark complexioned or Negroid, and they considered this consistency significant. Contrary to their observations, the syndrome has been seen in light-complexioned persons. Four of twenty-one patients reported by Dormandy had fair complexions, as did the patient described by Troxell. Other investigators have reported similar findings.

Microscopically, the pigment appears to be consistent with normal (physiologic) mouth pigment, the clinical location and distribution being the distinctive factors. Jeghers and associates were able to biopsy a palmar macule, and they noted that the pigmented particles occurred mainly in vertical bands throughout the epidermis. Biopsies performed by other investigators[64] failed to reveal any particular pattern that would delineate these lesions from other pigmented skin lesions on microscopic examination. Troxell, in a thorough histopathologic report, also does not confirm the "vertical band formation" as being characteristic of this syndrome. He noted a microscopic picture in the melanoplakia of the Peutz-Jeghers syndrome which was similar to that seen in normal or physiologic melanoplakia. One can expect to find increased infiltration of pigment cells in the basal layer and possibly an increased number of clear cells of Masson. Pigment granules also may occur in the dermis and upper epidermis; those in the dermis are generally chromatophores. Examination of a biopsy specimen from a mucosal lesion did not present any distinctive microscopic picture unique to the syndrome.

Much has been said concerning the similarity of the spots to ephelides (freckles). Freckles have a distribution pattern unlike that of the pigment spots in Peutz-Jeghers disease. They appear to be more numerous on the cheeks

and nose and less so around the mouth and nostrils, the extraoral areas most commonly affected in the Peutz-Jeghers syndrome. Light-complexioned persons are somewhat more susceptible to ephelides, which occur early in life but not in infancy. Freckles are more prominent during the spring and summer, and they apparently vary with exposure to sunlight. Freckles are never found on the palms of the hands or the soles of the feet.

In some of the earlier, unproved cases of the Peutz-Jeghers syndrome the possibility of Addison's disease was considered. The pigment here differs in that it is much more generalized over the entire body and is usually accentuated in the body folds.

Touraine and Couder refer to the pigmentary part of the syndrome as lentigo. Lentigines differ in that they are widely disseminated and have no particular predilection for the buccal mucosa. Also, there is no known hereditary predisposition.

Although no adequate proof is yet available, the pigment in the Peutz-Jeghers syndrome is generally conceded to be melanin.

GASTROINTESTINAL POLYPOSIS

The second cardinal symptom of the Peutz-Jeghers syndrome is intestinal polyposis. Raiford[54] defines an adenomatous polyp as "a benign hyperplasia of the glandular epithelium of the mucous membrane." Polyps of the gastrointestinal tract are most common in the large intestine; they occur less frequently in the stomach and are relatively rare in the small intestine. The polyposis in the Peutz-Jeghers syndrome is usually of a diffuse nature, being distributed throughout the intestinal tract. The most common site, however, is the small intestine. The other areas most often mentioned are the jejunum, ileum, duodenum, colon, rectum, stomach, and appendix. It is interesting to note that four of Peutz's patients had nasal polyps and one had polyposis of the urinary bladder. Jeghers and associates considered the presence of polyps in the small intestine a constant feature of the syndrome, and this continues to be commonly recognized and universally accepted today. Of twenty-one cases studied by Dormandy,[22-25] there were gastric polyps in four, polyps of the colon in eight, and rectal polyps in eleven. Twenty patients, however, had proved polyposis of the small intestine. In fifty-two cases reviewed by Statley and Schwartz,[64] there were polyps of the small intestine in forty-nine, while in the other three cases either such polyps were absent in this area or no information concerning their location was available. River collected fifty-nine cases and found gastric lesions in ten and colonic lesions in twenty; all fifty-nine patients, however, had polyps of the small intestine.

The symptoms presented by these patients are largely those referable to small-bowel intussusception. Usually the presenting complaint is of periodic, intermittent attacks of colicky abdominal discomfort which varies from slight cramps to a more severe, excruciating type of pain. Vomiting, diarrhea, anemia, weakness, and rectal bleeding are common accompanying symptoms. Clinically, the picture is that of obstruction of the small intestine. Sometimes the intussusception may be palpated in the abdomen. On occasion, rectal polyps may

prolapse through the anus and be seen clinically. Roentgenologic, sigmoidoscopic, and gastroscopic examination may aid in the diagnosis, although they are not always dependable.

Treatment is always surgical in nature, and many patients undergo multiple procedures for removal of the polyps. The literature reflects a great variety of ideas concerning therapy. These range from a rather conservative approach in which only symptomatic polyps are removed to prophylactic laparotomy wherever the typical melanotic spots are found. The latter procedure was recommended because of the possibility of future intussusception or malignancy. Most authors favor the former method, with possible resection of part of the bowel if a number of polyps are found in a short section.

The intestinal lesions are the usual adenomatous type of polyps found throughout the entire gastrointestinal tract. They appear to be of the type seen in generalized polyposis of the intestine without the pigmentary syndrome. The possibility of malignant degeneration of these polyps has been questioned by some investigators. Hereditary large-bowel polyps have been known to become cancerous; however, the potential of the lesions of the small intestine to degenerate is apparently small. Bockus,[14] Bjorkroth,[13] Struthers,[66] and Dormandy[22-25] believe that carcinomatous change in the small intestine is uncommon. Maingot[48] and Aird[1] believe that the lesions are potentially dangerous in this respect. Bartholomew and co-workers[6-7] believe that the polyps suggest developmental anomalies rather than true neoplasms. No metastases occurred in any of the seventy-five cases that they reviewed.

HEREDITARY ASPECTS

From the very beginning, the familial tendencies of this disease have been recognized. As noted earlier, Peutz studied three generations in a family of twenty and found that nine persons had the pigmentary pattern and that seven of the nine also had the polyps. Bruwer and associates,[15] Trengove-Jones,[71] Jeghers,[40-42] Dormandy,[22-26] and most other researchers observing this syndrome have noticed the familial trait. Some writers found sporadic cases, demonstrating that the disease is not always hereditary.[61, 63] The latter are fewer in number.

Investigation has shown that there is no doubt concerning the hereditary aspects of polyposis coli or multiple polyposis of the large intestine. The genetic pattern of the Peutz-Jeghers syndrome, although a unique entity in itself, demonstrates a similar pattern. The condition is said to be inherited as a simple mendelian dominant trait with a high degree of penetrance. A single pleiotropic gene is probably responsible for both characteristics of the syndrome (melanin spots and polyps). Both male and female carry the factor, and offspring of those who have the disease apparently have a 50 per cent chance of getting it. The sporadic instances must be the result of new mutations.

AGE AND RACIAL DISTRIBUTION

The syndrome has been diagnosed at opposite ends of the age scale. Cases have been reported in patients ranging in age from 3 to 77 years. It seems,

however, that the majority of the persons affected are in the second or third decades of life. Both sexes seem to be equally afflicted.

No one race or color appears to have a particular propensity for the disease or, for that matter, any immunity to it. The syndrome has been reported as in French, Italian, Hungarian, Polish, Jewish, Japanese, Chinese, Negro, Dutch, Norwegian, Turkish, Mexican, Spanish, Portuguese, Canadian, Indo-European, and American patients.

CASE REPORT

A 77-year-old white Jewish man was admitted to the hospital for the twelfth time, by way of the Emergency Ward, with the chief complaint of massive gastrointestinal bleeding.

Present Illness.—Prior to his hospitalization, he noted black stools and bright red blood following an enema. Shortly afterward, he vomited approximately 1,000 c.c. of blood. His hemoglobin on admission was 8.5 Gm., necessitating transfusion of two units of whole blood.

Past Medical History.—The patient had enjoyed good health until the age of 68, at which time he first sought medical care for acute abdominal pain. He subsequently was admitted to the hospital in 1950, and a diagnosis of pedunculated papillary carcinoma of the rectum, polyps of the sigmoid, and a bleeding ulcer was made. At this time the oral mucous membrane apparently was well hydrated and pale, with no sign of pathologic disease. Multiple colotomies were performed, and three polyps of the descending sigmoid colon were excised. The remainder of the descending and transverse colon, the ascending colon, and the cecum were negative on palpation. The liver showed no evidence of metastatic nodules. The stomach was essentially negative, and no distinct ulcer or ulcer crater could be found.

One month later the patient was readmitted for treatment of thrombophlebitis and emphysema. A bilateral superficial femoral vein ligation was performed.

In 1951 a bleeding duodenal ulcer was diagnosed, and a subtotal gastrectomy with anterior gastrojejunotomy was performed. Pathologic findings were negative at that time.

In 1952 he was hospitalized for a sigmoidectomy. The colon was entirely negative except for the lower end of the sigmoid and upper rectosigmoid, where a movable polypoid mass had formed. A polyp was defined and excised.

In 1953, 1954, and 1955 the patient was plagued with gastrointestinal hemorrhage of unknown cause. An active jejunal ulcer was discovered in 19[illegible]. In 1957 a carcinoma of the transverse colon was found and the colon was resected. Two other hospital admissions followed—one for a transurethral resection of the prostate and the other for treatment of an acute lower respiratory infection.

Family History.—The social history was essentially noncontributory. The patient denied any family history of heart disease, diabetes, tuberculosis, cancer, or mental disease. His father died of complications following pneumonia at the age of 75. His mother died at 25, following childbirth. One brother died in the Russo-Japanese War. Two sisters, aged 69 and 74, were living and apparently in good health; the patient had no children. Careful interrogation of the patient elicited no recognition of similar oral pigmentation in any of the patient's relatives, either living or dead.

Physical Examination.—The pulse rate was 80; respiration, 20; and blood pressure, 150/90.

The patient was a light-complexioned, well-developed, well-nourished man. His skin, which was normal in texture, was warm and dry with no sign of pigmentation on the face, trunk, or extremities. Sinus rhythm was normal; there were no cardiac murmurs, and the heart was not enlarged. The lungs were clear to percussion and auscultation. The abdomen, on which there were multiple scars, was distended slightly with increased bowel sounds. Rectal findings included tarry stool and 3-plus benzidine.

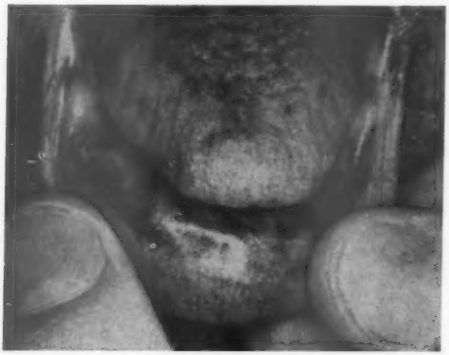

Fig. 1.—Heavy concentration of pigmentation on lower lip. The spots on the tongue are singular.

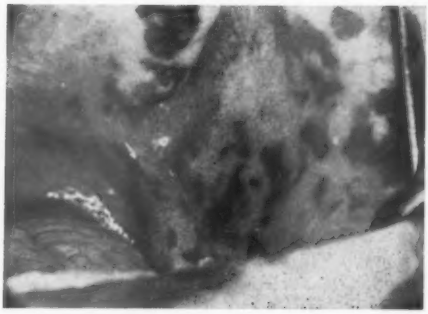

Fig. 2.—Large melanin patches on buccal mucosa and tuberosity area. Single pigment spots can be seen near the soft palate.

Fig. 3.—Characteristic spotting of buccal mucosa and lips. Note their presence in the retromolar pad area.

Oral Examination.—Multiple, small (2 to 4 mm. in diameter), well-defined pigmented areas were spread over the mucous membrane in the periphery of the lips and on the cheeks, the hard and soft palates, the edentulous tuberosity region of the maxillary ridge, the floor of the mouth, and the tongue. The concentration of pigment was more apparent near the lips and on the buccal mucosa. These irregular spots were not elevated, and they appeared to be black in color. The patient, who was considered a reliable historian, denied that these spots had been present prior to 1950 and suggested that their appearance had gradually increased in number since that time.

Fig. 4.

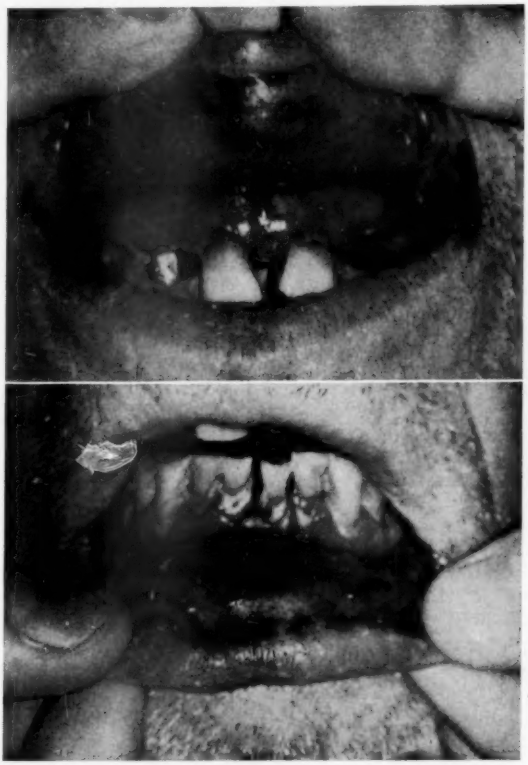

Fig. 5.

Figs. 4 and 5.—Heavy melanin deposits in the region of the upper and lower lips.

Laboratory Findings.—The laboratory data show a change in hemoglobin from 8.5 to 13.8 following multiple transfusions. All other tests (urinalysis, complete blood counts, and differential) were within the normal range.

X-Ray Findings.—Upper gastrointestinal examination showed swelling and some obstruction to the flow of barium in the efferent loop, with irregularity of folds at the stoma, probably caused by the previous operative procedures.

Barium enema and air-contrast examination of the sigmoid colon revealed a minute polypoid filling defect, measuring approximately 4 mm., which probably represented a sigmoid polyp. No other polyps could be identified at this time.

Another case of extensive oral pigmentation similar to that found in the Peutz-Jeghers syndrome was seen in a 38-year-old woman. Areas of pigmentation were noted on the buccal mucosa, tongue, palate, and lips. The patient first became aware of these spots approximately one year before she sought treatment. X-ray studies of the upper gastrointestinal tract revealed nothing of diagnostic significance. Further investigation for intestinal polyps was contemplated, but the patient did not return for the studies.

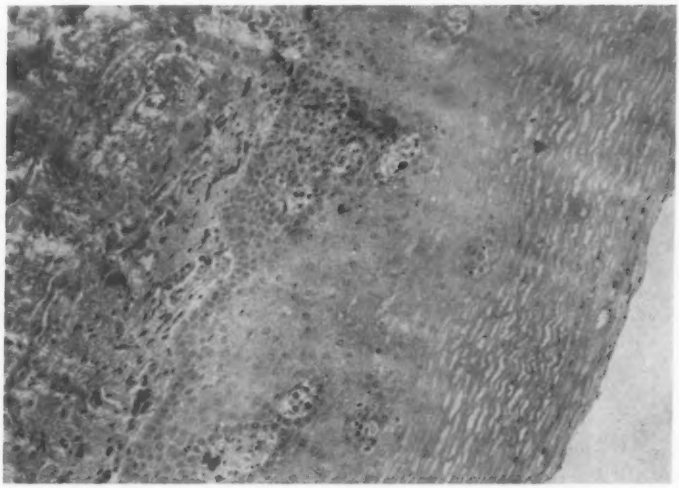

Fig. 6.—Photomicrograph of section taken from pigmented area of the buccal mucosa. Note abundance of pigment granules in the area directly below the basal layer.

DISCUSSION

In the past, interest has been aroused concerning conditions that manifest a type of oral pigmentation. The presence of such pigmentation as a physiologic or pathologic entity is of great importance to the dentist, as it offers a distinct aid in the diagnosis of many systemic conditions. Physiologic melanoplakia is seen in Negroes, dark-complexioned persons, and members of the yellow and brown races. Oral pigmentation that can be considered pathologic in nature can, for the most part, be divided into four groups on the basis of etiology:

1. Local causes (foods, heavy metals, drugs, etc.)
2. Systemic causes (Addison's disease, hemochromatosis, diabetes, tuberculosis, neurofibromatosis, disseminated lupus erythematosis, and many others).
3. Dermatologic diseases (particularly those involving marked cutaneous pigmentation).
4. Malignant growths (such as malignant melanomas).

The Peutz-Jeghers syndrome is another important systemic disease with melanoplakic manifestations. The typical oral pigmentation which is practically

pathognomonic of the disease is sometimes unrecognized or disregarded by both patient and physician. The brown spots on the buccal mucosa can easily be overlooked when the surgeon is faced with an acute abdominal condition. Because of the potential serious complications associated with it, it is imperative that this syndrome be recognized. Recognition of the characteristic pigmentation should lead to proper intestinal studies. In this respect, the dentist can certainly offer direct diagnostic aid.

SUMMARY

1. The literature pertaining to the Peutz-Jeghers syndrome has been reviewed, and the evolution of the disease has been traced.

2. This hereditary disease demonstrates a unique distribution of orofacial pigmentation along with generalized intestinal polyposis.

3. The symptoms, both local and systemic, have been discussed in detail.

4. The etiology of oral pigmentation has been discussed briefly, and the importance of the disease to the dental profession has been stressed.

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PHARMACOLOGY AND THERAPEUTICS

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TRIAMCINOLONE ACETONIDE

Subacute Toxicity Studies in the Rat

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TRIAMCINOLONE ACETONIDE (Kenalog),[1-4] a new synthetic corticosteroid, has been introduced to the professions for topical use in the treatment of dermal and oral mucous membrane lesions. Although minimal amounts of the corticosteroid are absorbed and available for systemic action following their application to the skin, that which is applied to the oral mucous membranes in the treatment of acute and chronic lesions is not only active locally but also ultimately may become more available for systemic activity as the result of absorption at the site of application or following ingestion.

Since little is known concerning the effects of orally administered triamcinolone acetonide, it seemed desirable to undertake a further "subacute" toxicity study in rats to investigate the drug's effects on various organ systems. This report is concerned with the results of such a subacute toxicity study which was made to ascertain the systemic effects of continued (ten-day) oral application of triamcinolone acetonide in an adhesive vehicle.

METHODS

Twenty young 200 gram male Sherman rats were divided equally into two groups:

Group I was composed of ten rats. Each animal was given a topical application of 20 mg. of a 0.1 per cent concentration of triamcinolone acetonide (in an adhesive vehicle, Orabase†) to the oral mucous membranes three times

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†The adhesive vehicle (Orabase) in which the triamcinolone acetonide was incorporated for purposes of this study contains gelatin, pectin, and carboxymethylcellulose in mineral oil-polyethylene base.

daily. The specific areas so treated were the mucobuccal fold, the gingivae, and the lower lip areas which directly overlie the lower incisor teeth. Thus, each animal received a total daily dose of 60 mg. of 0.1 per cent triamcinolone acetonide in Orabase or a total of 0.06 mg. of triamcinolone acetonide per animal per day (0.3 mg. per kilogram). This animal dose may be compared with the maximum anticipated human dose of 1.0 mg. per day for a 70 kg. person (0.014 mg. per kilogram of body weight). Therapy was continued for a period of ten days with an interruption of one day (Sunday) between the sixth and seventh days.

TABLE I. WEIGHTS OF ADRENAL GLANDS AND TESTES IN TEN CONTROL RATS AND FOLLOWING THE ADMINISTRATION OF A TOTAL DAILY DOSE OF 0.06 MG. OF TRIAMCINOLONE ACETONIDE PER ANIMAL TO TEN TREATED RATS OVER A PERIOD OF 10 DAYS

RAT	RIGHT ADRENAL WEIGHT (MG.)	LEFT ADRENAL WEIGHT (MG.)	BOTH ADRENAL GLANDS TOTAL WEIGHT (MG.)	TESTES WEIGHT (GM.)
		Group I		
1	11.0	10.0	21.0	2.580
2	11.0	13.0	24.0	3.020
3	8.8	10.0	18.8	1.640
4	14.0	17.0	31.0	2.620
5	15.0	15.0	30.0	2.110
6	14.0	12.0	26.0	2.600
7	10.6	12.0	22.6	2.100
8	11.0	15.8	26.8	2.440
9	12.0	13.6	25.6	2.670
10	8.2	10.2	18.4	1.260
Average	11.56	12.86	24.42	2.301
		Group II		
11	15.7	10.2	25.9	2.550
12	17.0	18.8	35.8	2.870
13	14.4	13.8	28.2	2.770
14	14.0	16.7	30.7	2.460
15	19.2	18.2	37.4	2.450
16	17.9	15.0	32.8	2.710
17	12.3	7.5	19.8	3.070
18	14.5	9.5	24.0	2.660
19	18.0	15.0	33.0	2.760
20	16.1	13.5	29.5	3.080
Average	15.89	13.82	29.71	2.732

Group II was composed of ten rats, each of which was treated in an identical fashion as those of Group I except that the placebo adhesive vehicle (Orabase) that was applied to the test site did *not* contain the active ingredient, triamcinolone acetonide.

Animals were weighed before and after treatment. The remainder of the data presented below were obtained at autopsy.

All animals were fed ad libitum on Hemlock Hollow rat diet. All medications were coded before being administered to the animals, thus ensuring a blind study throughout all stages of clinical observations, laboratory tests, and gross and histologic examinations of tissues at autopsy and thereafter.

RESULTS

Animals were killed at the end of ten days of treatment.

Aside from alteration in adrenal size, no other evidence of organ pathosis was noted at the time of autopsy upon examination of gross specimens. Autopsy weights of both the adrenal glands and the testes were obtained. The results of these studies are shown in Table I.

These data indicate that the adrenal weight was significantly depressed in the group treated with triamcinolone acetonide when compared with the control group; a similar trend was found also for testicular weight.

TABLE II. BODY WEIGHTS OF EXPERIMENTAL ANIMALS (FOLLOWING THE ADMINISTRATION OF 0.06 MG. PER DAY OF TRIAMCINOLONE ACETONIDE PER RAT) AND OF PLACEBO-TREATED CONTROL ANIMALS

RAT	INITIAL BODY WEIGHT (GM.)	FINAL BODY WEIGHT (GM.)
Group I. Treated with Triamcinolone acetonide		
1	190	196
2	222	242
3	174	183
4	202	208
5	165	185
6	170	188
7	157	168
8	188	202
9	224	232
10	180	178
Average	187.2	198.2
Group II. Controls		
11	206	243
12	198	244
13	158	200
14	194	233
15	214	247
16	185	225
17	156	208
18	157	205
19	180	224
20	178	204
Average	182.6	223.3
Average gain in body weight:		
Animals treated with triamcinolone acetonide		11.0 grams
Control animals		−40.7 grams

The "before and after" total body weights (in grams) of the animals in both groups are included in Table II. It was found that although the average weight of the animals in the group treated with triamcinolone acetonide was slightly higher at the outset than the weight of the animals in the control group, after ten days of therapy the average body weight of the triamcinolone acetonide group was significantly depressed as compared with that of the control group. The total gain in body weight over the ten-day period was 11 grams per animal for the group given triamcinolone acetonide as opposed to 40.7 grams for the control group.

At the time of autopsy, portions of the heart, lungs, liver, kidneys, spleen, reproductive organs, bone marrow, pancreas, gastrointestinal tract, and adrenal glands were removed for microscopic examination. Histologic study of these organs revealed the following: In the group treated with triamcinolone acetonide, one animal was observed to have a pneumonia, another had an anemic infarct of the liver, and a third animal showed a mild disorganization of the cellular distribution of the adrenal cortex. All of these changes, however, were considered to be unrelated to the experimental regimen since examination of the control animals revealed that three animals showed the same adrenal changes as the single animal in Group I in which adrenal changes had been noted. No other pathologic findings were noted.

DISCUSSION

Although deleterious histologic changes in the soft tissues of the treated rats were not apparent, these findings cannot be construed as being entirely indicative of negative findings for the body as a whole. Nor can these observations be interpreted as evidence that there were no clinical findings. Extreme care must also be taken in the projection of these data in rats to human subjects, since differences in terms of dose response in particular and of individual tissue response in general are often of great importance.

The corticosteroid doses used in this study were calculated to take into account the rat's inherent ability to adjust in general to larger doses of drugs without evidencing toxic effects as compared with man, the dosage factor usually applied being of the order of ten to one. An additional increment was added as a further safety factor to ensure more valid projection of data.

SUMMARY

The effects of the application of triamcinolone acetonide (Kenalog) 0.1 per cent in an adhesive ointment to the oral mucosa of the rat for ten days were studied with regard to weight gain, adrenal and testicular weights, and gross and histologic examination of the internal organs. The administration of 0.06 mg. of triamcinolone acetonide in divided doses per day to ten experimental rats (as compared to ten placebo-treated control rats similarly studied) revealed definite curtailment of gain in body weight, diminished adrenal weight, and a trend toward a diminished testicular weight in the animals treated with triamcinolone acetonide but no evidence of toxic effects as determined by gross and microscopic examination of the heart, lungs, liver, kidneys, spleen, reproductive organs, bone marrow, pancreas, gastrointestinal tract, and adrenal glands. It can be concluded that in this dose triamcinolone acetonide was active systemically but not organotoxic to the rats used in this experiment.

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ANESTHESIOLOGY

CARDIOVASCULAR RESPONSES TO LOCAL DENTAL ANESTHESIA WITH EPINEPHRINE IN NORMOTENSIVE AND HYPERTENSIVE SUBJECTS

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INTRODUCTION

For many years dentists have been adding epinephrine or some other vasoconstrictor to local anesthetics. The addition of a vasoconstrictor enhances the depth and duration of local anesthesia and reduces the rate of systemic absorption. Bleeding at the operative site is also reduced.

There is considerable disparity in views regarding the changes which may result from the use of vasoconstrictors in local anesthetics. Clough[1] found that in hypertensive patients the rises in blood pressure produced by epinephrine injections were much greater than those observed in normal subjects. Hickey[2] stated that cardiac complications, such as precordial pain or coronary thrombosis, when they occur, are caused by the vasoconstrictors in the anesthetic solution. Bloom[3] lists aortic regurgitation, mitral insufficiency, exophthalmic goiter, arteriosclerosis, and hypertension as contraindications to the use of epinephrine-containing local anesthetics.

In contrast, many workers have reported similar pressor responses in hypertensive and normotensive subjects. Fatheree and Hines[4] noted no distinct difference in the response of hypertensive and normotensive subjects to epinephrine. These findings were confirmed by Gordon and Levitt[5] and by Tainter and Winter.[6] Starr and co-workers[7] injected an average dose of 0.7 ml. epinephrine 1:1,000 (70 gamma) subcutaneously in patients. The diastolic pressure usually fell. Salman and Schwartz[8] reported that in patients with cardiovascular disease no untoward effects were observed after the injection of vasoconstrictors with local anesthetics. The New York Heart Association,[9] in a letter to the American Dental Association dated Oct. 5, 1954, states in part: ". . . The use of epinephrine with procaine for dental surgery presents no special hazards in persons with heart disease. We would recommend for any

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one session that there be used no more than 10 ml. of 1:50,000 epinephrine—no more than 0.2 mgm. of epinephrine in any form." It further cautions that a detailed history of the nature and severity of the patient's heart disease and information concerning any medication that the patient is receiving or has received should be available from the physician.

The evidence concerning the pressor reactivity of epinephrine in local anesthetic solutions is conflicting. There are no reports which analyze the cardiovascular changes that occur during oral surgery under local anesthesia with and without epinephrine.

The purposes of this study were (1) to investigate the possible pressor and other cardiovascular effects of the injection of 2 per cent lidocaine with and without epinephrine 1:100,000 and (2) to investigate these parameters following the extraction of teeth under local anesthesia with and without epinephrine. The study, which was performed on subjects with frank hypertension, follows pilot studies done on dogs by Nakauchi[10] and on selected normotensive human subjects by McCarthy.[11]

METHOD OF INVESTIGATION

This study was made on twenty-six patients in the Department of Oral Surgery of the District of Columbia General Hospital. The subjects were chosen from ambulatory and nonambulatory outpatients of the cardiac clinic who exhibited clinical hypertension and/or cardiac disease associated with hypertension. Patients were selected on the basis of blood pressure readings of 150 mm. Hg systolic and 90 mm. Hg diastolic as the upper limit of normal. The limits of blood pressure were consistently elevated to avoid patients with only labile hypertension. All patients showed at least Grade II hypertensive retinopathy according to the classification of Keith, Wagener and Barker.[12] Detailed medical studies, including electrocardiograms, had been made of the patients selected. The patients were divided into two groups. Group I consisted of six ambulatory subjects from the outpatient dental clinic. They were currently in good health and had no history of cardiovascular disease or of past illnesses which could conceivably affect the results of the study. Each was given a 2 ml. injection of 2 per cent lidocaine plain and subjected to extraction of a maxillary tooth. Each of the same six normotensive subjects then received a 2 ml. injection of 2 per cent lidocaine with epinephrine 1:100,000, after which a maxillary tooth was extracted. This group was used as a control. Group II was composed of twelve Negro men and eight Negro women with hypertensive cardiovascular disease. Five of these patients had myocardial infarction, the most recent being five weeks and the latest three months postinfarction. The patients ranged in age from 35 to 69; the average age was 47.2 years. Each patient was questioned carefully regarding hypertension and previous hospitalization, dental surgery, medications, and possible allergic reactions. Each of the hypertensive patients received an injection of 2 ml. of 2 per cent lidocaine plain and underwent the extraction of a maxillary tooth. Later, 2 ml. of 2 per cent lidocaine with epinephrine 1:100,000 was injected and a maxillary tooth was extracted.

A 5 ml. syringe of the lock type with a sharp 1 inch 25 gauge needle was used routinely for injection purposes. The sites of injection were the submucous maxillary mucobuccal fold region and the submucous posterior palatine region. The choice of sites was pertinent, since the posterior palate region is extremely sensitive to pain. Any cardiovascular response initiated by the pain stimulus of the penetrating needle would thus be reflected in all cases treated. Five minutes after injections were given, a maxillary posterior tooth was extracted by the forceps technique.

It is held generally that the basal blood pressure is the value obtained after sixty minutes' rest in the supine position. Normal resting blood pressure and heart rate were determined on each subject over a sixty-minute period. The patient was instructed to lie quietly on a stretcher. The electrocardiogram electrodes were applied during this rest period. A preoperative electrocardiogram was obtained on each patient before treatment. Blood pressure was determined by the auscultatory method with an aneroid sphygmomanometer over the right brachial artery. Heart rate was determined by counting the pulse at the left temporal artery for thirty seconds and multiplying by two. While lacking in accuracy, this served as a comparison for the heart rate which could be determined from the electrocardiographic tracing as follows: Several R-R intervals were counted, and the number of 0.2 second intervals over the same distance were counted. The rate was then calculated by the following formula:[13]

$$\frac{\text{Number of R-R intervals} \times 300}{\text{Number of 0.20 intervals}} = \text{heart rate per minute}$$

After a standard twelve-lead electrocardiogram was obtained preoperatively, lead II was monitored continuously, beginning thirty seconds before and ending five minutes following the injection and extraction procedures. The electrocardiographic method of analysis was used in order that fleeting systemic effects which could not be observed with intermittent blood pressure and pulse determinations would not be missed.

The effects of the injection, the drug, and the subsequent tooth extraction on the systemic blood pressure, heart rate, and electrocardiographic complex were observed and recorded. Blood pressure and heart rate were determined at intervals of one-half, one, two, and five minutes after the injection and after the extraction procedure. Measurements were also recorded ten minutes after surgery was completed, while the patient was still in the supine position.

RESULTS

Resting values for blood pressure and heart rate were determined in normotensive and hypertensive patients in an attempt to establish a norm for the test subjects prior to actual treatments. The resting level means of this experiment approximate average values for normotensive and hypertensive subjects, although they are subject to wide individual variations. The values presented in Table I represent the means of all the absolute values obtained during rest.

TABLE I. RESTING BLOOD PRESSURE AND PULSE DETERMINATIONS

	BLOOD PRESSURE		PULSE RATE PER MINUTE
	SYSTOLIC (MM. Hg)	DIASTOLIC (MM. Hg)	
Normotensive patients	126 ± 12.3	76 ± 10.9	88 ± 12.8
Hypertensive patients	177 ± 13.6	103 ± 8.9	83 ± 11.7

The range of changes in cardiovascular functions observed at the most significant time intervals during the initial period of rest and following the drug injection and tooth extraction, respectively, is presented in Tables II and III. The systemic arterial pressure and pulse responses of the normal and hypertensive groups to the different drug injections and subsequent tooth extractions are shown in Figs. 1 and 2.

TABLE II. MEAN PRESSOR CHANGES FOLLOWING INJECTION AND EXTRACTION IN NORMOTENSIVE PATIENTS

	AFTER INJECTION				AFTER EXTRACTION				
	30 SEC.	1 MIN.	2 MIN.	5 MIN.	30 SEC.	1 MIN.	2 MIN.	5 MIN.	10 MIN.
Lidocaine 2 Per Cent									
Systolic (mm. Hg)	129	129	129	125	138	135	130	126	125
Diastolic (mm. Hg)	74	73	73	74	80	81	78	75	74
Pulse rate per minute	87	86	88	88	89	87	86	83	82
Lidocaine 2 Per Cent With Epinephrine 1:100,000									
Systolic (mm. Hg)	135	134	132	130	139	135	131	129	128
Diastolic (mm. Hg)	80	79	77	77	76	77	76	76	75
Pulse rate per minute	92	94	91	92	93	90	90	88	86

When the rises in blood pressure and pulse rate only are considered, the following observations may be made: (1) in general, the greatest average rise in systemic arterial pressures and pulse rate occurred immediately after tooth extraction under lidocaine plain in all groups; the rise was somewhat higher in the hypertensive group than in the normotensive group. (2) In both groups, when lidocaine with epinephrine was used, there was a greater average rise in systemic arterial pressures and pulse rate immediately after injection than somewhat later; the rise was considerably higher in hypertensive patients than

TABLE III. MEAN PRESSOR CHANGES FOLLOWING INJECTION AND EXTRACTION IN HYPERTENSIVE PATIENTS

	AFTER INJECTION				AFTER EXTRACTION				
	30 SEC.	1 MIN.	2 MIN.	5 MIN.	30 SEC.	1 MIN.	2 MIN.	5 MIN.	10 MIN.
Lidocaine 2 Per Cent									
Systolic (mm. Hg)	189	189	187	181	198	189	182	180	177
Diastolic (mm. Hg)	104	102	102	101	106	104	102	102	101
Pulse rate per minute	86	87	86	87	88	86	85	83	82
Lidocaine 2 Per Cent With Epinephrine 1:100,000									
Systolic (mm. Hg)	198	195	192	192	205	196	190	185	184
Diastolic (mm. Hg)	107	104	102	103	108	105	103	104	102
Pulse rate per minute	96	88	87	87	90	88	87	85	84

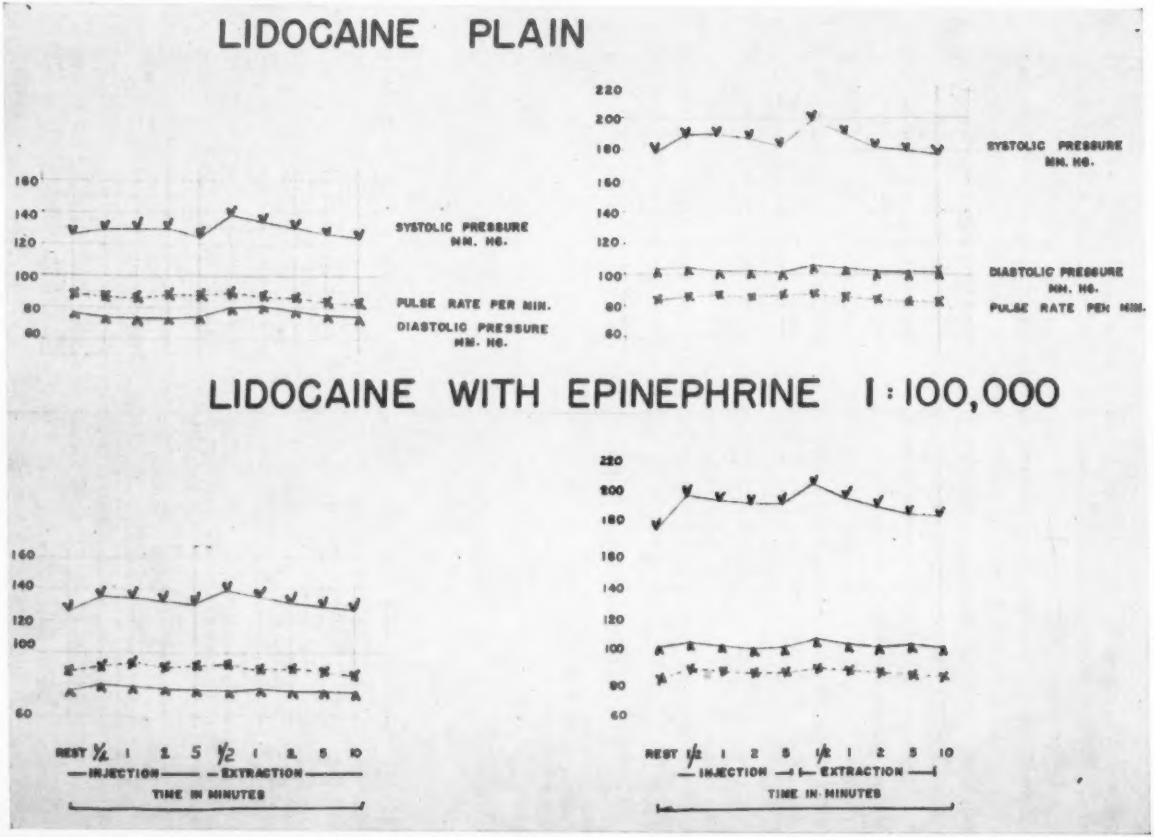

Fig. 1.

Fig. 2.

Figs. 1 and 2.—Alterations in heart rate in normotensive (Fig. 1) and hypertensive (Fig. 2) patients.

in the normotensive group. (3) When the rises produced by both solutions are considered, there was no statistically significant variation for the groups. Whereas the rises occurred immediately after injection of lidocaine with epinephrine, there was a proportionate lesser rise immediately after dental extraction. This rise was in the same magnitude as that produced immediately after extraction under lidocaine plain in both groups, although a lesser rise occurred immediately after injection in these cases.

When the decreases in blood pressure only are considered, we find that in both groups the greatest average fall occurred in the diastolic pressures somewhat less frequently after lidocaine plain than after lidocaine with epinephrine. This fall was greater immediately after injection than after dental extraction where only rises were noted.

When the increases and decreases in blood pressure and pulse rate are considered in combination, the following observations may be made: (1) In both groups (normotensive and hypertensive) there was a decrease in average systemic pressures and pulse rate from that *immediately* after the injection and after the extraction to those five minutes after injection and extraction, respectively. (2) In all groups (except normotensive patients given lidocaine without epinephrine) there was a mean value rise in systemic arterial pressures and pulse rate immediately after the injection. (3) In all groups there was a mean value rise in systemic arterial pressures and pulse rate immediately after tooth extraction. (4) The percentage of patients who experienced a rise in systolic blood pressure immediately after injection was greater than the percentage in which there was a fall or no change. This tendency was generally maintained at the one-minute interval but not at the five-minute interval. (5) There was a greater percentage of patients in all groups who experienced a rise in diastolic blood pressure and pulse rate immediately after injection than those in whom there was a fall or no change. This tendency was generally maintained at the one-minute interval but not at the five-minute interval. (6) In all groups there was a greater percentage of persons who experienced a rise in systemic arterial pressures and pulse rate immediately after extraction than those who experienced a decrease or no change. This tendency was generally not maintained at the two-minute interval and was completely absent at the ten-minute interval.

Analysis by Comparison With Standard Deviations.—Considering the analysis of pressor and heart rate changes obtained after injection and after extraction with the resting level standard deviations for all patients and all treatments, there is lack of statistically significant variation.

Alterations in Cardiac Rhythm.—These were evidenced in the electrocardiographic tracings. The alterations in heart rate have been described and are graphically shown in Figs. 1 and 2. Fig. 3 illustrates some of the more consistent alterations in rhythm seen in normotensive and hypertensive patients.

Premature contractions (PVC's) of two types—ventricular and auricular (atrial)—were identified. PVC's were less frequent when the epinephrine-free

Figs. 1 and 2.—Alterations in heart rate in normotensive (Fig. 1) and hypertensive (Fig. 2) patients.

local anesthetic was used. Normotensive as well as hypertensive patients manifest this alteration in cardiac rhythm. In those patients who exhibited PVC's in the preoperative electrocardiogram, actual tabulation indicated more frequent PVC's after injection and especially after extraction. The latter was more evident when epinephrine was used in conjunction with lidocaine. Hypertensive patients differed from normotensive persons quantitatively rather than qualitatively. Nine of twenty hypertensive patients and two of the six normotensive patients had PVC's.

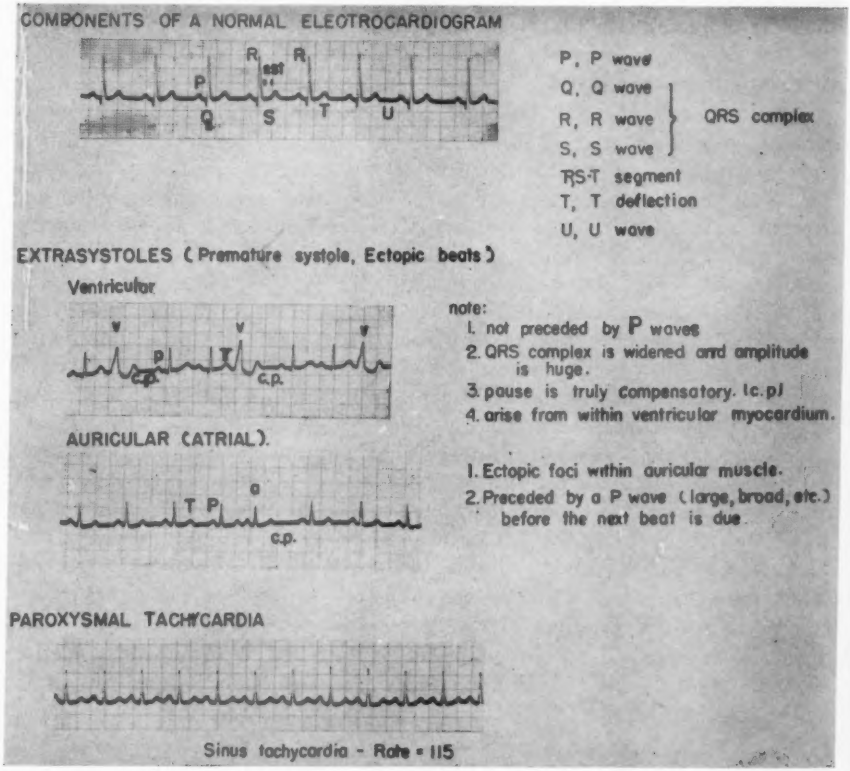

Fig. 3.—Electrocardiographic findings. Sinus arrhythmias were present occasionally but not consistently.

Paroxysmal tachycardia was recorded on two hypertensive patients and one normotensive patient. The preoperative electrocardiogram demonstrated a tachycardia present before treatment.

In both groups sinus arrythmias were present occasionally during the procedure but not consistently.

Alterations in Electrocardiographic Complex.—Specifically, this would include such changes as RS-T segment alterations, T-wave inversion, and abnormal

QRS complex. No significant variations in the electrocardiographic complex were produced by injection and/or extraction in either the control or the epinephrine-treated groups of normotensive and hypertensive patients.[14]

DISCUSSION

Cardiovascular Response to Lidocaine Plain and Tooth Extraction.—The cardiovascular responses of the six normotensive and twenty hypertensive patients given 2 ml. lidocaine without epinephrine and subjected to tooth extraction was uniform and striking. The greatest percentage of pressor changes occurred immediately following dental extraction (Tables II and III).

The pressor changes that occur immediately following the injection of solution are most probably psychosomatic in origin, being related to fear of injection. Extensive studies in man and animals[15, 16] have shown that anxiety, apprehension, fear, and excitement tend to increase systemic arterial pressure, particularly the systolic phase, and to increase the heart rate. McCarthy,[11] in his work on normotensive patients, demonstrates a definite blood pressure and pulse rate response to the injection itself and not to the test solution or the injection site. However, the injection sites are worthy of comment. Injections in the posterior palatine region are more painful than injections in the maxillary mucobuccal fold because the submucosa at the mucobuccal fold consists of loose connective tissue which is architecturally arranged so as to tolerate injections with minimal pain stimuli. The palatine submucosa, on the other hand, is thin, firm, inelastic, and closely adherent to the underlying periosteum. The pain factor at the latter site was obvious during actual testing. Considering the factors of both the pain attending the actual injections and the patient's psychosomatic response to fear of injection, an increase in systemic arterial pressure and heart rate is understandable and expected.

The cardiovascular responses of the hypertensive patients to this treatment differed from those of the normal subjects quantitatively rather than qualitatively. The responses of the former were characterized by a more marked elevation of systemic arterial pressure and frequently by an increase in heart rate.

Cardiovascular Response to Lidocaine With Epinephrine and Subsequent Tooth Extraction.—The cardiovascular responses of the six normotensive and twenty hypertensive patients given 2 ml. of lidocaine with epinephrine 1:100,000 and subjected to tooth extraction were uniform and striking. The greatest percentage of pressor changes occurred immediately following the injection of solution into the maxillary mucobuccal and posterior palatine regions.

Whereas the pressor and pulse changes occurred earlier when epinephrine was used with the anesthetic, the over-all pressor changes (that is, the total rise in systemic arterial pressure and pulse rate) were almost identical for the control and the epinephrine groups. The mechanism for the relatively slight rise or decrease in diastolic pressure is the depressor action of epinephrine in small amounts.[16] This results from peripheral vasodilatation and decrease of peripheral resistance. It should be noted also that the absorption of solution is more

rapid from the posterior palatine injection than from a mucobuccal injection. Koppanyi[17] speaks of this area of injection as being comparable to an intravenous injection, since systemic absorption is so rapid.

The cardiovascular responses of the hypertensive patients to local anesthesia with epinephrine differed from the responses of the normotensive patients and from the control subjects quantitatively rather than qualitatively. The responses of the hypertensive patients were characterized by a more marked elevation of the systemic systolic pressure and frequently by a corresponding rise in the heart rate. This was expected, since it is known that hypertensive persons are hyperreactors to epinephrine[18] and in addition, as mentioned previously, are more reactive than normotensive persons to pressor stimuli in general.

The classical pharmacologic conception of the pressor action of epinephrine is that it depends chiefly on intense vasoconstriction, direct cardiac action being a lesser factor. Barker,[13] however, states that at times epinephrine has the undesirable effect of producing ventricular extrasystoles and, less often, ventricular tachycardia and fibrillation.

The hypotensive action of epinephrine in small doses, reported as early as 1900 and extensively studied by Cannon and Lyman[19] and by McCarthy[11] in normotensive dental students, has been generally regarded as being of minor physiologic importance. Whereas elevation of diastolic pressure is a characteristic feature of essential hypertension, epinephrine caused an insignificant increase in diastolic blood pressure in normotensive subjects. The diastolic pressure was decreased in hypertensive patients. I attribute the concomitant rise in systolic blood pressure to increased cardiac activity (caused by pain and psychic fear of injection) and the relatively slight rise or decrease in diastolic pressure to decreased peripheral resistance and vasodilation. Epinephrine cannot be regarded as the only agent responsible for this phenomenon, however, since increased sympathetic activity would appear to be an important mechanism.

No untoward effects were observed, either in the patients with hypertension or in the normotensive groups, after the injection of lidocaine with epinephrine and subsequent tooth extraction. Some isolated clinical manifestations, such as pallor, tremor, and nervousness, were probably caused by the pain of the injection or extraction, by psychic reaction, or possibly by the systemic effect of the drug. Such phenomena are transitory and are observed in patients without disease as well as in patients with hypertension and heart disease. There were no signs of excitement, syncope, sweating, or other allergic manifestations to the local anesthetic agent.

The patients who received lidocaine with epinephrine and underwent subsequent tooth extraction presented clinical evidence of diminished postoperative bleeding from the socket wound. This was determined from the condition of the gauze sponges placed over the sockets. In addition, the patients so studied attested to the depth and duration of anesthesia produced.

It has been stated many times in the past that the use of local anesthetic solutions without epinephrine is unrealistic since the oral operations that follow are often associated with pain. This pain, in turn, will produce more epinephrine

from natural secretion (adrenal medulla) than does the 1:50,000 or 1:100,000 epinephrine normally used in local anesthetic solutions. It is true that depth of anesthesia is desirable. However, as has been demonstrated in twenty-six patients, both normotensive and hypertensive, an anesthetic properly placed by infiltration or by the block method will produce satisfactory anesthesia for routine dental procedures within five minutes.

The pressor response related to fear of the injection and the impending dental surgery was so evident in this experiment, and also in those reported by Cheraskin and Prasertsuntarasai,[20] that premedication should become routine when local anesthesia for dental procedures involving trauma is anticipated for patients with hypertension, cardiovascular disease, and anxiety states. These patients are greater operative risks, and care should be taken to see that their physical abnormalities are recognized. The care of patients of this type necessitates close cooperation between the physician and the dentist. Anxiety, apprehension, pain, fear, or prolonged traumatic operations should be avoided. Adequate preoperative medication, usually with barbiturates as the drugs of choice, is therefore important to ensure a smoother and safer surgical procedure.

SUMMARY

From a study in which office dental procedures were simulated, the cardiovascular responses (pressor, heart rate, and electrocardiogram) of hypertensive and normotensive patients to 2 per cent lidocaine with and without epinephrine and to maxillary tooth extraction were determined.

Resting level blood pressure and pulse rate determinations approximating the accepted values for normotensive and hypertensive persons have been reported. Electrocardiographic tracings were obtained on all patients before the tooth extractions and to monitor the treatment procedure continuously.

It is evident that the patients, after reclining in the treatment room and anticipating dental surgery, show a rise in systemic arterial pressure and pulse rate immediately after injection and after extraction. This was probably due in a large measure to the attending pain of the treatment procedures plus psychosomatic fear of the injection and the extraction.

In general, the cardiovascular responses of the hypertensive patients differed from that of the normal subjects quantitatively rather than qualitatively. It was characterized by a rise in the systolic pressure and heart rate and frequently by a slight rise or fall in the diastolic pressure. Hypertensive patients were shown to react more vigorously to pressor stimuli. The lack of significant variations in the magnitude of pressor changes between the normotensive and the hypertensive subjects in response to lidocaine plain and lidocaine with epinephrine 1:100,000, with the exception of a mild systolic rise in the hypertensive group given lidocaine with epinephrine, has been indicated.

No significant variations in cardiovascular responses (blood pressure, heart rate, and electrocardiographic complex) were produced by injection and/or extraction in either the control or the epinephrine-treated groups of normotensive and hypertensive patients.

CONCLUSIONS

Local anesthetic solutions containing therapeutic amounts of epinephrine can be used without fear of complication in patients with hypertension.

The author gratefully acknowledges the assistance of Drs. Gustav O. Kruger, John C. Rose, and Walter C. Hess.

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ORAL ROENTGENOLOGY

American Academy of Oral Roentgenology

Arthur H. Wuehrmann, Editor

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RADIATION PROTECTION VIA THE PINHOLE CAMERA

Albert G. Richards, M.S., Ann Arbor, Mich.*

NEW knowledge can be obtained sometimes by the application of old ideas to new problems. The truth of this statement will be illustrated here by the results obtained when the principles of the pinhole camera were applied to present-day problems involving x-radiation in dentistry.

During the past few years, many techniques have been suggested to keep to a minimum the amount of x-radiation to which both the patient and the operator are exposed in the dental office. The following measures are suggested for the protection of the dental patient against needless exposure to x-radiation:

1. Use of high-speed film.
2. Full development of film.
3. Limitation of the diameter of the x-ray beam to the smallest practical size by means of a lead diaphragm.
4. Passing of the x-rays through a filter to remove the nonuseful radiation from the beam.
5. Operation with high voltages.
6. Use of an extended distance between the x-ray tube and the patient's face.

To keep the irradiation of the dentist or other dental personnel to a minimum, the following suggestions are made:

1. Avoiding exposure of one's body (including the hands) to the primary or useful x-ray beam.
2. Securing a longer cord for the x-ray timer so that the operator can stand well away from the patient during each exposure.
3. Staying behind a barrier to radiation if suggestions 1 and 2 cannot be followed.

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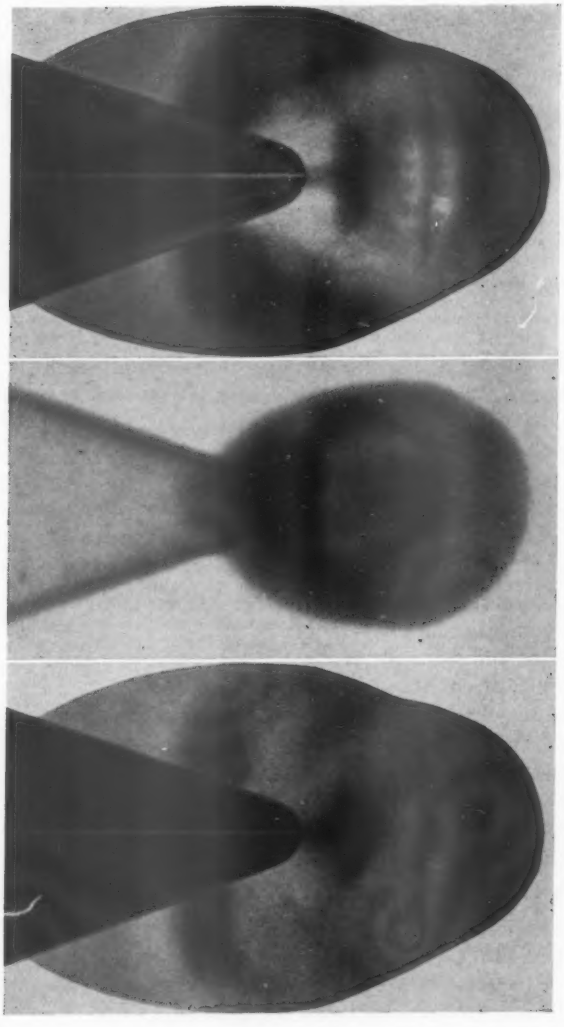


C.

B.

A.

Fig. 1.

An additional suggestion to be presented in this article will complete the preceding lists.

Many remember the old-fashioned box camera which consisted of a light-tight box with a lens and shutter in the center of its front surface. A sheet of film was located inside the box along the back surface. If we were to alter the box camera by replacing the lens and shutter with a pinhole, that box camera then would become a pinhole camera capable of producing photographs that exhibit very good detail and a great depth of focus. A drawback to the use of the pinhole camera is that the exposure times are very long. As the pinhole is made smaller, the picture becomes clearer, but the time required for exposure increases rapidly. Any visible radiation that reflects off a subject in a direction suitable for passing through the pinhole of the camera will produce an image on the film. The image will be inverted and reversed on the film, just like images produced by conventional cameras.

If a pinhole camera were made of lead and loaded with roentgenographic film, it could be used to produce a new type of roentgenogram.[1, 2] The conventional type of roentgenographic image is produced by radiation from an x-ray tube after that radiation has been attentuated by the various tissues which it has encountered while passing through the subject.

The roentgenogram made with the pinhole camera differs from the conventional roentgenogram in that it is produced by the x-radiation that originates within the subject. Every particle of matter that is exposed to the primary beam of an x-ray machine emits secondary x-rays which scatter in all directions. The secondary rays, which the subject is emitting in directions suitable for passing through the pinhole of the camera, can be used to produce this new type of roentgenogram. An object in the dental office emits secondary radiation only while it is being irradiated by the primary x-ray beam.

When a lead-lined pinhole camera is loaded with a sheet of photographic film and a sheet of roentgenographic film located between intensifying screens, photographs and roentgenograms can be made simultaneously of any subject that is emitting x-rays and reflecting visible rays of light.

Since exposures made with pinhole cameras are very lengthy, it is not biologically advisable to use this equipment in its present stage of development on living patients. Therefore, a phantom, which consisted of a human skull filled and coated with a material equivalent to tissue, was used in the experiments which now will be reported.

A dental x-ray machine was positioned in relation to the phantom as though the region of the maxillary central incisor were to be examined. The pinhole camera, loaded with both photographic and roentgenographic films, was positioned directly in front of the phantom. The pinhole of the camera was located in the median sagittal plane, at the level of and 6 inches from the anterior nasal spine of the phantom. Fig. 1, *A* shows the photographic image that was recorded by the pinhole camera. Since the pinhole of the camera was so close to the phantom and the x-ray cone, the perspective of the photograph is greatly exaggerated. Fig. 1, *B* represents the roentgenographic image that was recorded simultaneously by the pinhole camera. This roentgenogram shows

that the cone and a small volume of the patient emit scattered secondary radiation. The volume of the patient that emits the secondary radiation is the same volume that is irradiated by the primary x-ray beam. Apparently, far more secondary radiation is produced by the soft tissues than by the teeth and alveolar bone.

By superimposing views *A* and *B* of Fig. 1, it is possible to relate the position of the normally invisible sources of the secondary radiation to the visible details in the photograph (Fig. 1, *C*). Roentgenograms of the patient's eyes are of no diagnostic value to a dentist; therefore, there is no justification for the unnnecessary irradiation of eyes. Suitable restrictions on the size of the primary x-ray beam can prevent some of the unnecessary irradiation of structures adjacent to the oral region. If the operator or some other person were standing in a position to achieve the same viewpoint as the pinhole camera, he would be irradiated by the secondary radiation which scatters from the pointed x-ray cone and the face of the patient. This position of the operator (behind the head of the x-ray machine) would not be considered very safe unless the vertical angulation of the x-ray beam were very low. With a low or small vertical angulation, the physical bulk of the head of the x-ray machine would act as a barrier to the secondary radiation that would normally reach the body of the operator. Even under these special conditions, only those portions of the operator's body that would lie in the "shadow" of the head of the x-ray machine would be protected from the scattered secondary radiation.

The roentgenograms made with the pinhole camera were produced under extreme conditions. The highest-speed roentgenographic film and intensifying screens were utilized. The x-ray machine was operated at its maximum voltage and current. The amount of exposure necessary to produce Fig. 1, *B* and the other similar pictures was about 100,000 times the exposure that normally is utilized, with the same conditions of voltage and current, to produce a periapical roentgenogram of the maxillary central incisor region of the living patient.

The positions of the pinhole camera in Figs. 1, 3, 4, and 5, relative to the phantom and the x-ray machine, are shown in Fig. 2.

The photograph in Fig. 3, *A* was made with the pinhole camera moved to the appropriate position indicated in Fig. 2. The relationship between the phantom and the x-ray machine remained unchanged. Fig. 3, *B* represents the various sources of secondary radiation which scatter in the direction of the pinhole when the camera has been moved to this new location. The superimposition of views *A* and *B* of Fig. 3 produces Fig. 3, *C*, which relates the position of the normally invisible sources of the secondary radiation to the visible details in the photograph. A visual comparison of Figs. 1, *B* and 3, *B* indicates that it would not be less hazardous for the operator to stand at the side of the x-ray machine than behind it.

Fig. 4, *A* pictures the phantom in profile. This new location of the pinhole camera is indicated in Fig. 2. Fig. 4, *B* which is the roentgenogram of the phantom's profile, clearly indicates that it is the soft tissues and not the hard tissues that produce the major amount of the scattered secondary radiation in the patient. Views *A* and *B* of Fig. 4 are combined to produce Fig. 4, *C*. A

visual comparison of Fig. 4, *B* with Figs. 1, *B* and 3, *B* indicates that it would be far safer for the operator to stand at a right-angle position, with respect to the primary x-ray beam, than at either of the two positions previously mentioned.

A rule for determining the operator's safety from secondary radiation exposure at a given position is that if he can see the area of the patient that is being irradiated by the primary x-ray beam this area also can "see" him and will expose his body to secondary radiation. It always must be remembered that the operator of a dental x-ray machine should never stand in the path of the primary x-ray beam, even if the head of the patient is situated between the x-ray tube and the body of the operator. Some of the primary radiation does pass through the head of the patient. If this statement were not true, it would be impossible to produce extraoral roentgenograms of a patient's head.

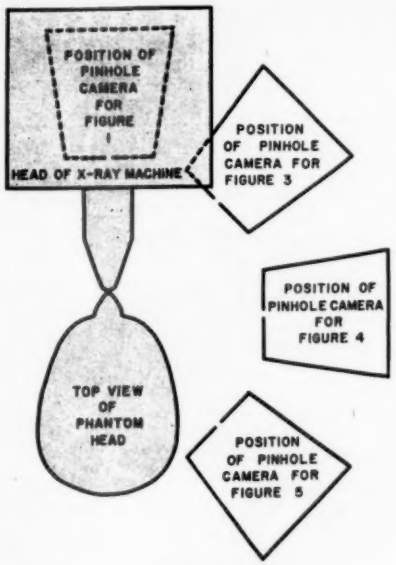
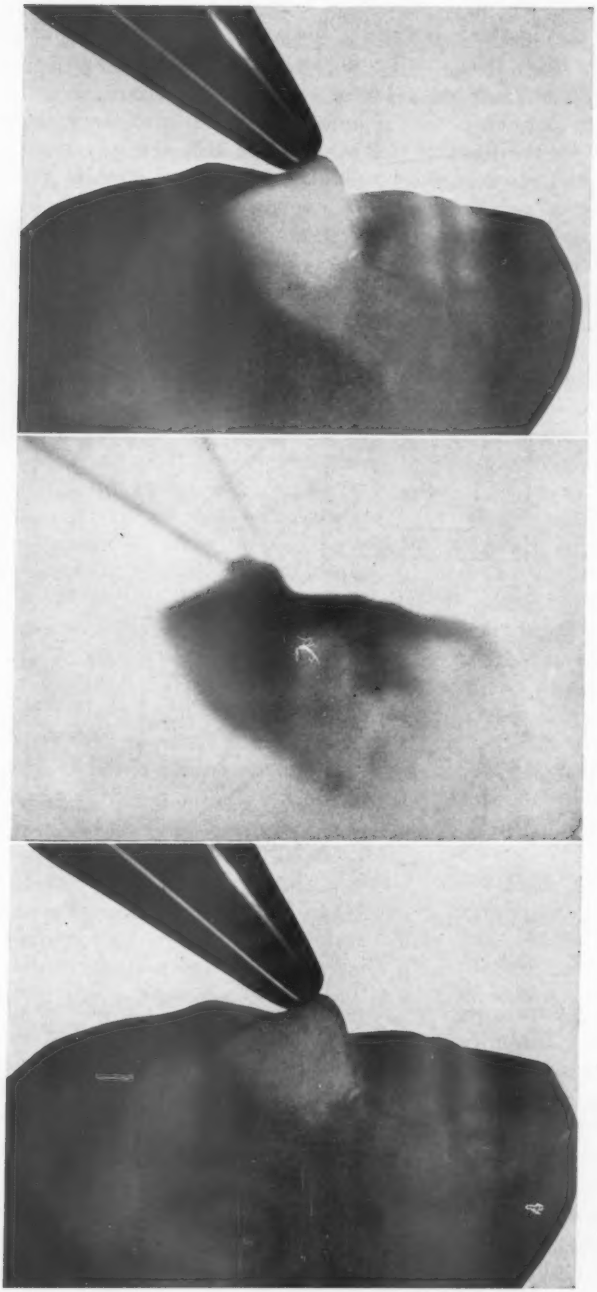

POSITION OF PINHOLE CAMERA FOR FIGURE 1
HEAD OF X-RAY MACHINE
POSITION OF PINHOLE CAMERA FOR FIGURE 3
POSITION OF PINHOLE CAMERA FOR FIGURE 4
TOP VIEW OF PHANTOM HEAD
POSITION OF PINHOLE CAMERA FOR FIGURE 5

Fig. 2.

It is difficult to orient the viewpoint from which the photograph in Fig. 5, *A* was made, a difficulty that arises because the phantom has no ears. Reference to Fig. 2 will help to clarify the location of the pinhole camera. The roentgenogram in Fig. 5, *B* illustrates the point that very little secondary radiation scatters from the patient to the pinhole camera at this location. It also shows that only that part of the pointed cone which emits secondary radiation is irradiated by the primary beam. A strong circular source of secondary radiation is indicated at the upper right border of the roentgenogram. The secondary radiation which caused this circular spot emerged through the aperture in the lead diaphragm. It originated in the filter and in other parts of



C.

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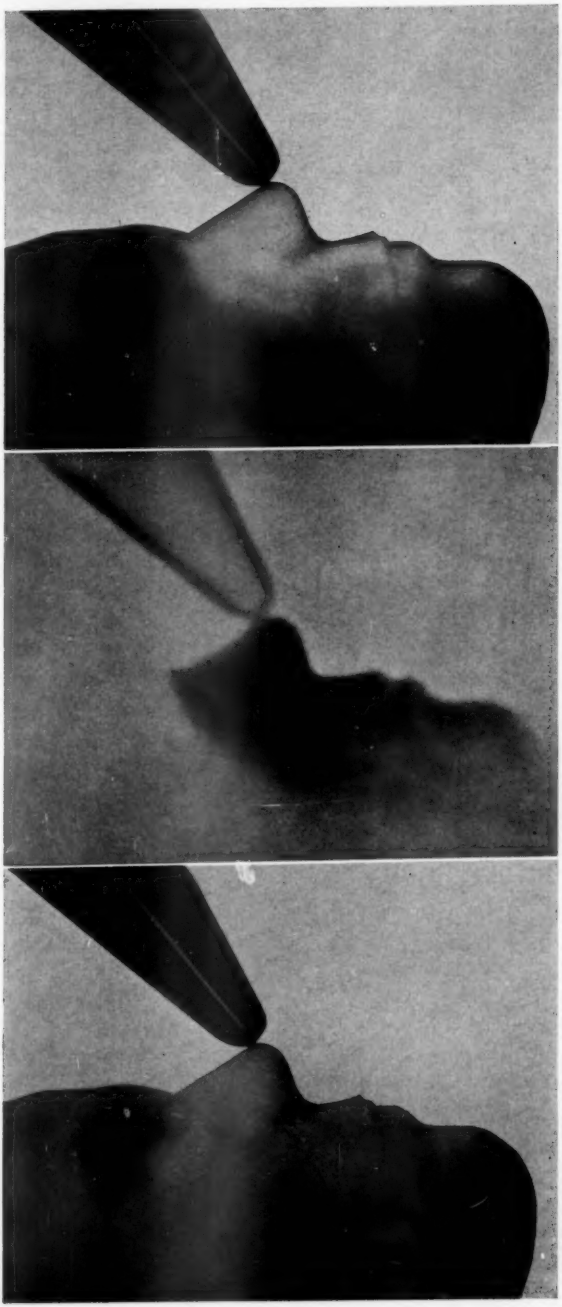
Fig. 3.



C.

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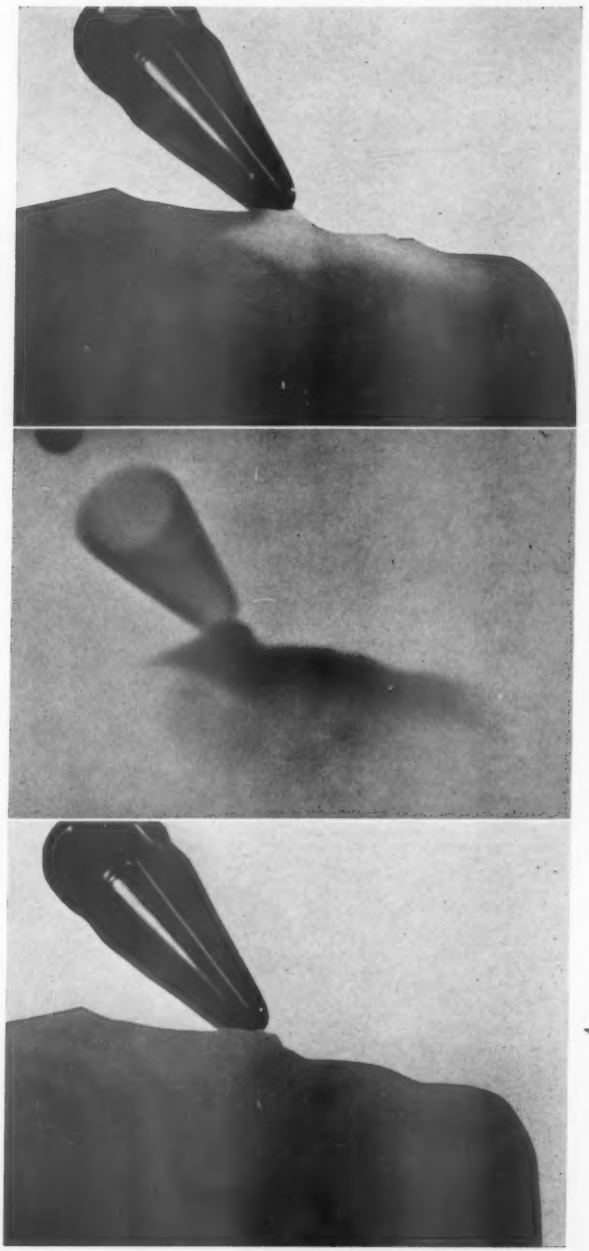
Fig. 4.



C.

B.

A.

Fig. 5.

the x-ray machine, located behind the lead aperture, which are strongly irradiated by the primary beam. This position of the operator would be the safest of all if the scatter from the cone and the scatter through the aperture were not present. Since these sources of secondary radiation do exist, however, and are present in most dental x-ray machines, this position of the operator would have to be classified as being about equal in safety to the right-angle position previously discussed.

When parts *A* and *B* of Fig. 5 are superimposed to produce Fig. 5, *C*, an interesting phenomenon becomes apparent. Only the tip of the phantom's nose is visible on the photograph. Yet, a much larger portion of the nose is disclosed by the secondary radiation which has passed through the phantom's right cheek. Apparently, secondary radiation from the patient is of quite a penetrating nature.

Fig. 6.

To produce the roentgenogram presented in Fig. 6, the pinhole camera was located at a position corresponding to the lap of a patient. This film has recorded all of the sources of secondary radiation which expose the gonadal region of the patient. The various sources of this scattered radiation can be divided into three groups. The first includes the chin, face, and nose of the patient; the second is the pointed cone; and the third is the secondary radiation which emerges through the circular aperture in the lead diaphragm. Immediately above the large circular area on the roentgenogram is seen a small area which

is the image of the focal spot of the x-ray tube. The image of the focal spot is caused by leakage of radiation and not by secondary radiation. Very little leakage of radiation has occurred, as evidenced by the faintness of the image of the focal spot.

Measurements were made to determine the fraction of the total gonadal exposure that comes from each of the three groups of sources of secondary radiation. It was found that the chin, face, and nose contributed about 45 per cent, the pointed cone about 25 per cent, and the radiation through the aperture about 30 per cent of the total exposure of the gonadal region under the conditions of this experiment.

The intensity of the scattered radiation which came from the pointed cone and through the aperture was 0.5 to 1 per cent of the intensity of the primary beam when measured at equal distances from the aperture. The primary radiation was measured along the central ray of the primary beam, whereas the scattered radiation was measured at a 45 degree angle to the central ray.

The quality of the radiation scattered from each of the three groups of sources was measured and compared with the quality or penetrating ability of the primary beam. The quality of radiation is expressed as a number representing the half-value layer (HVL). This number is simply the thickness of a layer of aluminum that is required to reduce the intensity of the radiation by 50 per cent. The penetrating ability of the radiation increases with the HVL. Compared with the HVL of the primary beam, the HVL of the radiation from the phantom was slightly higher; for the radiation from the filter and other structures behind the diaphragm, it was slightly lower; and it was much lower for the radiation from the pointed plastic cones.

Although the radiation which is scattered from the pointed cone and through the opening in the lead diaphragm is not very intense, it does expose unnecessarily large areas of the patient's body. If these two sources of scattered radiation could be eliminated, the exposure of the patient's gonadal region could be reduced by 55 per cent when the maxillary incisor region is being radiated. Lesser reductions in the exposure of the gonadal region and the rest of the body would result when other regions of the oral cavity were examined.

Previous experiments have indicated that all of the secondary radiation from pointed plastic cones can be eliminated by using open-end cones. The diameter of the primary x-ray beam must be maintained slightly smaller than the inside diameter of the open-end cone, so that the cone is not irradiated by the primary beam.

Additional experiments have indicated that the area exposed to the secondary radiation which emerges through the aperture of the lead diaphragm can be reduced greatly by positioning the filter deeper inside the head of the x-ray machine, that is, farther from the lead diaphragm and closer to the x-ray tube. It is impossible to change the position of the added filter in many of the dental x-ray machines in use today; therefore, the alternative would be to use an open-end cone made with roentgenopaque walls. This latter suggestion would limit the area of the patient's skin that is exposed by secondary radiation from the filter to almost the same small area that is exposed by the primary x-ray beam.

Therefore, to complete the earlier lists of suggestions for promoting protection from x-radiation for the patient and the dentist, the following suggestion should be added: "Use an open-end cone with walls made of radiopaque material." As an alternative or an addition, the use of the double diaphragm and the repositioning of the x-ray tube and filter in the tube housing has been suggested.[3]

SUMMARY

A pinhole camera which simultaneously produces photographs and roentgenograms of any object which reflects light and emits secondary x-radiation has been described. Photographs and roentgenograms of a phantom's head, obtained with the pinhole camera and an x-ray machine, show the sources of secondary radiation which function when an examination of the patient's teeth is made by means of x-radiation. A method has been suggested for reducing the unnecessary exposure of both the patient and operator to scattered, secondary radiation.

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RECURRING SUPERNUMERARY MANDIBULAR PREMOLARS

Report of a Case of Postmature Development

Guy H. Poyton, F.D.S., H.H.D., George A. Morgan, D.D.S., F.A.C.D., and Stuart A. Crouch, L.D.S., D.D.S., Toronto, Ontario

WITH the increasing trend toward complete dental roentgenograms in the oral examination, it has been found that supernumerary premolars are more common than former estimates indicated. This can be accounted for by the fact that 75 per cent of the supernumerary premolars are impacted and generally unerupted. Their incidence is about one in 10,000 persons. The most common supernumerary teeth, listed in the order of frequency of occurrence, are central incisors, molars, premolars, cuspids, and lateral incisors. Some of the complications associated with them are delayed eruption, noneruption, separation, and malposition of the permanent teeth. Early removal of these teeth may be a means of avoiding the majority of these complications. One characteristic of mandibular supernumerary premolars is a marked tendency toward the formation of cysts.

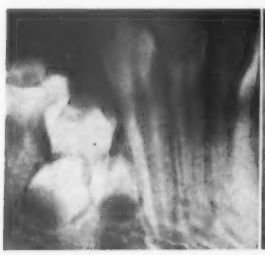

Fig. 1.

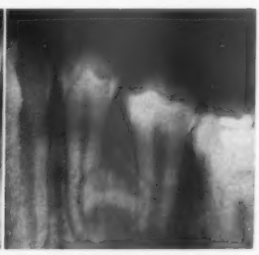

Fig. 2.

Fig. 1.—Preoperative roentgenogram taken in 1944 showing suppressed left mandibular permanent first premolar and two impacted supernumerary left mandibular premolars.

Fig. 2.—Preoperative roentgenogram taken in 1944 showing right mandibular permanent first premolar and impacted supernumerary right mandibular premolar.

CASE REPORT

Patient S. A. C., an 11-year-old girl, was referred to us by an orthodontist in September, 1944. We were asked to remove the suppressed left mandibular permanent first

From the Department of Radiodontics, Faculty of Dentistry, University of Toronto.

premolar and the two impacted supernumerary left mandibular premolars shown in Fig. 1, as well as the right mandibular permanent first premolar and the impacted supernumerary right mandibular premolar illustrated in Fig. 2.

Figs. 3 and 4 show roentgenograms taken immediately after complete removal of these permanent and supernumerary premolars.

Fig. 3. Fig. 4.

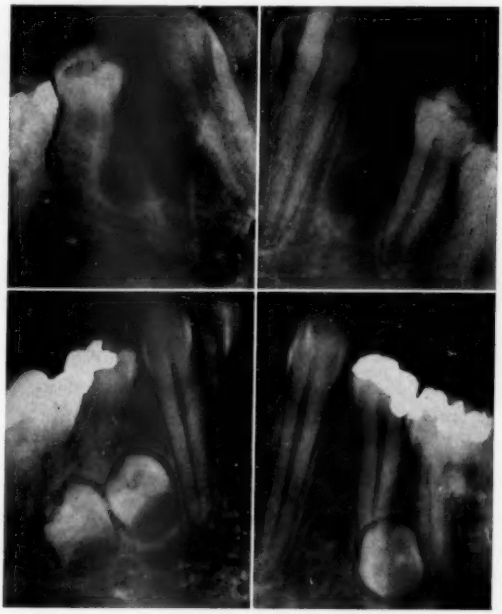

Fig. 5. Fig. 6.

Figs. 3 and 4.—Roentgenograms taken in 1944 immediately after complete removal of permanent and supernumerary premolars shown in Figs. 1 and 2.

Figs. 5 and 6.—Roentgenograms taken in 1949, five years after removal of first set of supernumerary premolars. Note recurrence of impacted supernumerary teeth.

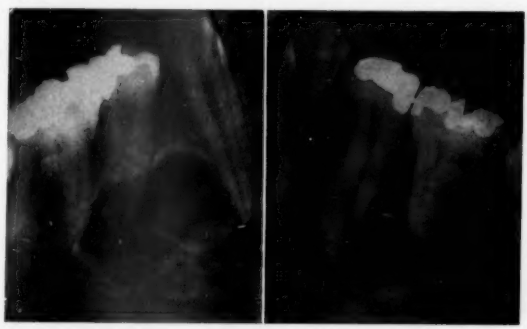

Fig. 7. Fig. 8.

Figs. 7 and 8.—Roentgenograms taken in 1949 immediately after removal of second set of supernumerary teeth.

Roentgenograms of the right and left mandibular premolar regions taken five years after removal of the first set of supernumerary teeth (Figs. 5 and 6) showed recurrence of the supernumerary premolars. As before, there were now two impacted supernumerary premolars on the left side and one impacted supernumerary premolar on the right side of the mandible. These teeth were removed completely, as shown in Figs. 7 and 8.

Other roentgenograms taken in 1949 disclosed the existence of two left maxillary supernumerary premolars which were not present in 1944 (Fig. 9). These teeth also were extracted (Fig. 10).

Fig. 9. Fig. 10.

Fig. 9.—Preoperative roentgenogram taken in 1949 shows two supernumerary left maxillary premolars that were not present in 1944.

Fig. 10.—Postoperative roentgenogram taken in 1949 immediately after removal of the supernumerary teeth shown in Fig. 9.

COMMENT

The foregoing case is most unusual in that three impacted supernumerary mandibular premolars in an 11-year-old girl, which were removed in September, 1944, were found five years later to have recurred (Figs. 5 and 6). In addition, two supernumerary premolars in the left maxilla, which were not present in 1944, were found in September, 1949. It is interesting to compare the size and shape of the first group of premolars seen in 1944 with the second group seen in 1949.

This case represents a total of eight impacted supernumerary premolars seen and removed over a span of five years.

ROENTGENO-QUESTIONS

Which target-skin distance, the 8 inch or the 16 inch, requires the least amount of radiation at the patient's skin to produce a film of the same density? If there is a difference, how great is it?

Basically, the greater the tube-patient distance, the less is the skin dose. This effect is produced through the spreading of the x-rays from the target. The dose variations in the beam can be calculated by applying the inverse-square law. For accuracy corrections must be made for increased air absorption on the part of the 16 inch distance and increased tissue backscatter on the part of the 8 inch distance. However, these corrections are of less importance than the application of the inverse-square law. Let us consider a case in which are used two x-ray beams having (1) the same film-to-skin distance of 2 inches, (2) the same diameter of irradiated skin of 2.75 inches, (3) the same x-ray dose of 100 mr applied to the film, (4) approximately the same tissue absorption of x-rays, and (5) the same KVP. By applying the inverse-square law, we find that the 8 inch target-to-skin distance will produce a skin dose of 156 mr, while the 16 inch distance will produce a skin dose of 127 mr.

This effect can be demonstrated mathematically. Assuming X amount of radiation at 1 inch from the tube target for the 8 inch technique and 4X for the 16 inch technique (a quadrupling of quantity is needed for a doubling of the distance), one can compute the fraction of the initial radiation that will reach the skin. The skin-to-film distance is constant—arbitrarily 2 inches. The strength of the x-ray beam at the film will be constant in both cases:

$$\frac{(1'')^2}{(8'')^2} \times X = \frac{1}{64} X; \frac{(1'')^2}{(16'')^2} \times 4X = \frac{1}{64} X$$

The strength of the x-ray beam at skin distance will not be constant:

$$\frac{(1'')^2}{(6'')^2} \times X = \frac{1}{36} X; \frac{(1'')^2}{(14'')^2} \times 4X = \frac{1}{49} X$$

The literature is deficient in data pertaining to depth and exit doses in oral roentgenography; thus, a proper evaluation of the difference in the roentgen hazard of the two techniques cannot be made.

The American Academy of Oral Roentgenology solicits from the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY any questions which deal with technical or interpretive aspects of oral roentgenology. These questions should be sent directly to the editor of this section, Dr. Arthur H. Wuehrmann, School of Dentistry, University of Alabama Medical Center, Birmingham, Alabama; the editor will distribute them for reply to a suitable group within the Academy. Questions, with the answers, will be published at as early a date as possible in "Roentgeno-Questions." Questions, especially those of an interpretive nature, should ordinarily be accompanied by good-quality roentgenograms and a pertinent history. The names of the questioner and the respondent will not be published.

ROENTGENO-ODDITIES

Technical Errors

Errors in intraoral roentgenographic techniques are not oddities, since they are made every day by dental practitioners. There is an increasing need for reducing radiation through improved techniques, however, and it is important that the practitioner recognize the causes for the technical errors that he may have produced.

Fig. 1 demonstrates the error of leaving in an acrylic partial denture during roentgenographic examination of the cuspid and lateral teeth. We know that the partial denture is acrylic, since the denture base material does not show roentgenographically. Both vulcanite and metal offer resistance to the x-rays; the latter, of course, is totally roentgenopaque. In this instance it is obvious that the caries on the distal side of the cuspid can be observed only minimally and that possible caries on the mesial side of the cuspid is obstructed.

Fig. 2 shows the stretched effect of the trabecular pattern and is indicative of film curvature. The patient should not be allowed to hold the film so close to the tissues that the film curves. This may be compared with Fig. 3, which shows an actual creasing of the film in the upper right-hand corner. Such creasing is ordinarily done deliberately for tissue relief. Deliberate bending of the film corners should be kept to a minimum; it is ordinarily not necessary, and, if it is necessary, only the extreme corner of the film should be rounded for the patient's comfort.

Fig. 4, a lower molar film, demonstrates the result of film overlapping in the developing solution. The lighter area, having the shape of a portion of film, was caused by another film sticking to the one which we observe during the developing process and preventing full action of the developing solution. The film was then washed and fixed properly. Had this overlapping occurred in the fixer rather than in the developer, incomplete fixing and a resultant oxidation stain would have resulted.

Each month this section will bring to the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY one or more roentgenograms which demonstrate unusual, unexpected, rare, or bizarre roentgenographic changes. These roentgenograms will be accompanied by an explanation or by words of inquiry regarding the particular change. All films used in this section will be accepted with the understanding that 2 by 2 or 3¼ by 4 inch slides or glossy photographs of the films will be made available to interested readers through the editor of the American Academy of Oral Roentgenology at the individual's expense. The cost will involve only the photographer's charges. Each slide or print will give credit to the donor. Interesting roentgenograms are solicited from all sources. Please be certain to identify your films properly so that they can be returned. All material for publication should be submitted to Dr. Arthur H. Wuehrmann, University of Alabama School of Dentistry, Medical Center, Birmingham, Alabama.

Fig. 5 shows the overlapping of interproximal spaces, which results from improper horizontal angulation and an inability of the x-rays to pass directly through the interproximal spaces. Diagnostically, these films are valueless as far as caries is concerned and are generally ineffective for other pathologic entities.

Fig. 1.

Fig. 2.

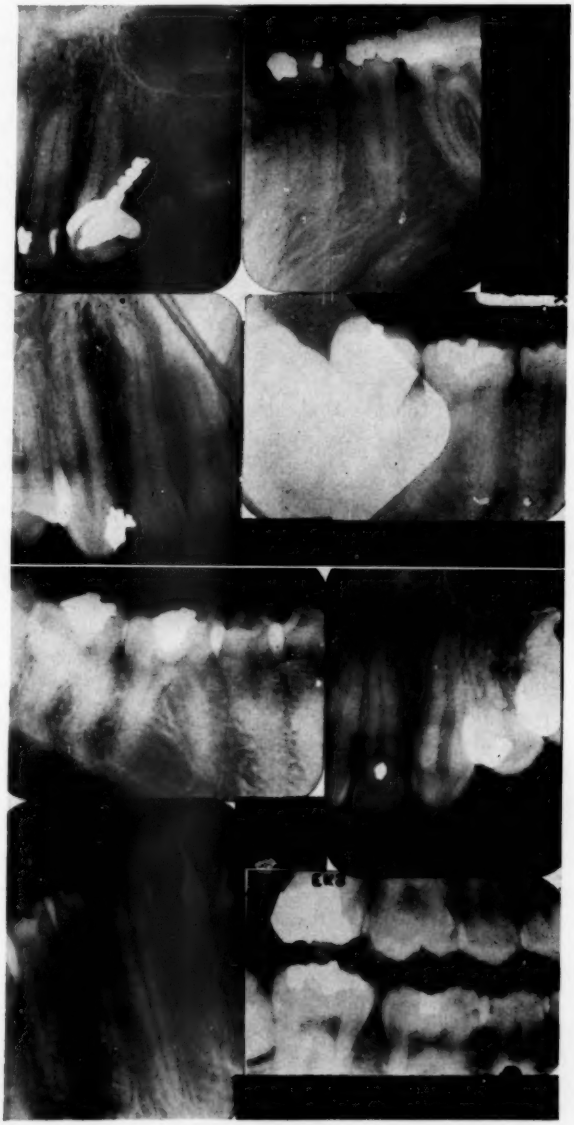

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

Fig 7.

Fig. 8.

Fig. 6 demonstrates overlapping of the premolar and cuspid; the cause is commented upon in Fig. 5. In addition, the vertical angulation used was excessive, resulting in a foreshortening of the teeth and a casting of the supportive bone well up onto the crown surfaces. The reader will note that the actual level of bone on the lateral tooth is a little more than halfway up the root from the apex, but another layer of bone can be seen close to the cementoenamel junction. This layer is not anatomically present but is cast close to the crown of the tooth through excessive vertical angulation. The identification of the excessive vertical angulation can also be made by observing that the buccal cusp of the premolar is considerably longer than the palatal cusp Under proper angulation circumstances, these cusp tips would be superimposed, since anatomically they are almost equal in length.

Fig. 7 illustrates insufficient vertical angulation and probably some film curving which, in combination, produce elongation of the teeth. In addition, the long axis of the teeth is not aligned with the vertical borders of the film, and the teeth appear to be crossing the film.

Fig. 8, a bitewing film, again demonstrates improper horizontal angulation. The reader will observe that all the interproximal spaces, with the exception of the area between the mandibular first and second molars, show overlapping. While some caries of a relatively extensive nature can be observed, it is entirely probable that smaller interproximal areas have been obliterated as a result of the overlapping. Radiation must be used wisely and effectively. Such films do not produce optimal diagnostic results.

Author's name withheld by request.

ORAL PATHOLOGY

MALIGNANT MELANOMA PRIMARY IN THE ORAL CAVITY

James F. Smith, B.S., D.D.S., Ph.D., Memphis, Tenn.*

MALIGNANT MELANOMA in the oral cavity is a very rare finding. Over a period of fifteen years only four cases have been reported in our study at the University of Tennessee Institute of Pathology. This tumor, according to cases reported, occurs most often in white patients; however, all four cases in our study occurred in Negro patients. The average age was 52 years. In all four of these cases there were no malignant changes other than those in the oral cavity, and junctional activity was present in all lesions.[1]

In the oral cavity the malignant melanoma usually presents marked pigmentation with poorly defined margins and possible ulceration.[2]

Microscopically, the changes that suggest malignancy include an increase in the size of the nuclei, an increase in the size of many cells with various shapes, prominence of nucleoli, and the presence of abnormal amounts of melanin both within the cells and outside the cells. These changes occur at the junction between the epidermis and the dermis, as well as extending into underlying structures.

The malignant melanoma disseminates widely and may involve any organ. When this tumor occurs in the oral cavity, a careful evaluation must be made of possible bone involvement. The treatment of choice in most oral lesions is wide excision, with therapeutic excision of regional and cervical nodes.[3] The prognosis of the malignant melanoma is poor, regardless of location and node involvement.[4]

The photomicrographs in Figs. 1 and 2 are from a malignant melanoma in a 54-year-old Negro woman who came to the clinic for treatment of a dark blue papillary lesion, 3.5 cm. in its greatest diameter, with a known duration of nine months. The tumor was located in the area of the left maxillary cuspid and was quite firm. The microscopic appearance was one of marked pleomorphism of cells, with many bizarre sizes and shapes of nuclei and nucleoli. There was hyperchromatism, and pigment could be seen outside as well as

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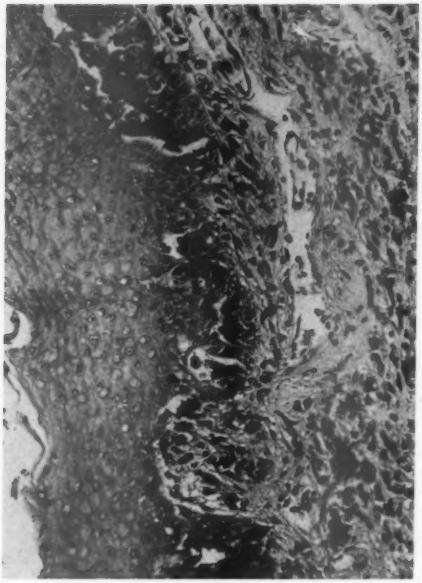

Fig. 1.—Malignant melanoma of the maxillary gingival tissue. Note melanoblastic activity at the dermal-epidermal junction.

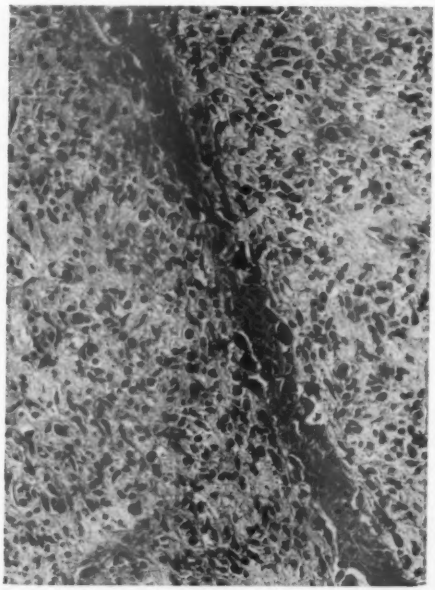

Fig. 2.—Section taken from deep in the dermal layer demonstrating melanoblastic activity.

within the cells. Mitotic figures were numerous. The tumor had invaded well into the dermis, and bony involvement was a necessary consideration even though there was no gross evidence of it. The tumor had extended over the edentulous alveolar ridge and onto the hard palate, so that the treatment of choice was wide excision.

CONCLUSION

Because of the grave prognosis and the danger of this tumor, any lesion that has the characteristics of malignant melanoma should be carefully examined and evaluated by the clinician and the pathologist.

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3. Sharp, G. S., Bullock, W. K., and Hazlet, J. W.: Oral Cancer and Tumors of the Jaws, New York, 1956, The Blakiston Company, p. 195.
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PERIPHERAL GIANT-CELL GRANULOMA

A Review of Twenty Cases

James F. Smith, B.S., D.D.S., Ph.D., Memphis, Tenn.*

THE peripheral giant-cell granuloma has been described in the literature, under various names, for many years. I prefer the term "granuloma" to "tumor" or "epulis," as the latter are misleading. These growths are reparative in the true sense of the word, and they are thought to be usually a response to injury.

Trauma from prior extractions, chronic irritation, and chronic inflammatory response are important in the etiology of the peripheral giant-cell granuloma. In eleven of the twenty cases studied, however, none of the above causes existed and the etiology was undetermined.

The tumor occurs on the gingiva. In the majority of our cases the base was pedunculated, although some may present a sessile type of base. It is necessary to study this tumor microscopically to differentiate it from the fibroma, lipoma, and reparative granulation tissue. An important differential point is the depth of tissue involvement, since this tumor arises from deeper structures, such as the periodontal membrane.[1]

The histologic features of the lesion are most interesting. The tumor is usually made up of connective tissue that appears immature. There are spindle-shaped fibroblasts with delicate fibrils. Vascularity varies, but in the majority of cases investigated here the tumors were quite vascular, with a history of frequent bleeding from trauma. Inflammatory cells were found consistently, in varying degrees. Bony spicules are often seen, as well as attempts at new bone formation. Giant cells are seen in varying sizes and numbers, and their origin is thought by some to be osteoclastic.[2]

The probable origin of this tumor is hemorrhage followed by proliferation of connective tissue and capillaries. Later, giant cells and bone formation may be seen.

The tumors discussed here involved very little invasion of bone. When bone is involved, careful evaluation must be made for possible sarcoma or endocrine disease.

The treatment of the peripheral giant-cell granuloma is complete excision, since this lesion has a tendency to recur when not completely excised. If the

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Fig. 1.—Typical giant cells seen in the peripheral giant-cell granuloma.

Fig. 2.

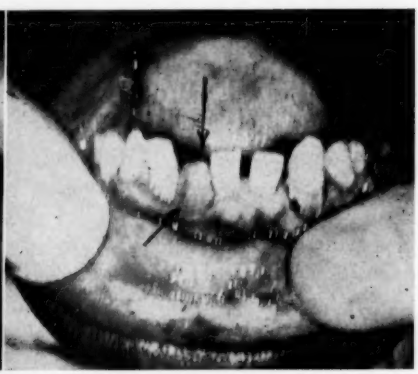

Fig. 3.

Fig. 2.—Peripheral giant-cell granuloma of the maxilla.
Fig. 3.—Peripheral giant-cell granuloma of the mandible.

periodontal membrane is involved and mobile teeth are present, it may be necessary to extract these teeth and thoroughly curette the granuloma.

TABLE I. REVIEW OF GIANT-CELL GRANULOMA CASES

Number of Cases	20
Sex	
Male	7
Female	13
Average age	
Males	32
Females	34
Site	
Maxilla	13
Mandible	7
Base	
Pedunculated	16
Sessile	4
Condition	
Ulcerated	5
Nonulcerated	15
History of Trauma	
Yes	9
No	11
Race	
Negro	12
Caucasian	8
Average diameter of tumor	1.2 cm.

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AN ORAL BENIGN LESION PROGRESSING TO EPIDERMOID CARCINOMA WITH METASTASIS TO THE LUNG

Report of a Case

James F. Smith, B.S., D.D.S., Ph.D., Memphis, Tenn.*

THE role of precursor lesions, which are initially benign but which may become malignant, has long been recognized. In the case reported here, however, it was possible to follow a specific benign lesion that was biopsied six years prior to its progression to epidermoid carcinoma.

Before the case is reported, however, certain terms used in this article should be defined.

Hyperkeratosis is a thickening of the corneous layer of the epidermis without remarkable changes in the underlying layers.

Leukoplakia is probably one of the most abused terms in the medical fields. The word implies only a white plaque occurring on the surface of mucous membranes, which can be quite misleading when we consider the number of lesions that may demonstrate this characteristic. We prefer that the lesion be diagnosed as to whether or not dyskeratosis is present. By *dyskeratosis* we mean the irregularity of maturation of cells from the basal-cell layer upward, pleomorphism with bizarre sizes and shapes of cells, and the presence of abnormal keratinization.[1]

Parakeratosis is the persistence of nuclei in the keratin cells, probably due to the rapidity of the keratinizing process in the stratum corneum.

Acanthosis is an increase in the number of cells in the prickle-cell layer. This may cause a thickening of the entire epidermis.

Epidermoid carcinoma, when well differentiated, consists of sheets and nests of cells that resemble squamous epithelium and have distinct cell membranes. The nuclei may vary in size and shape and stain heavily. Mitotic figures will also vary in number and may appear atypical. Keratin pearls of varying sizes may be seen in the dermis and epidermis.[2]

CASE REPORT

The patient, a 56-year-old white woman, had used snuff for a period of twenty-five years and stated that she had always held the snuff in the same position in the mouth. There

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Fig. 1.

Fig. 2.

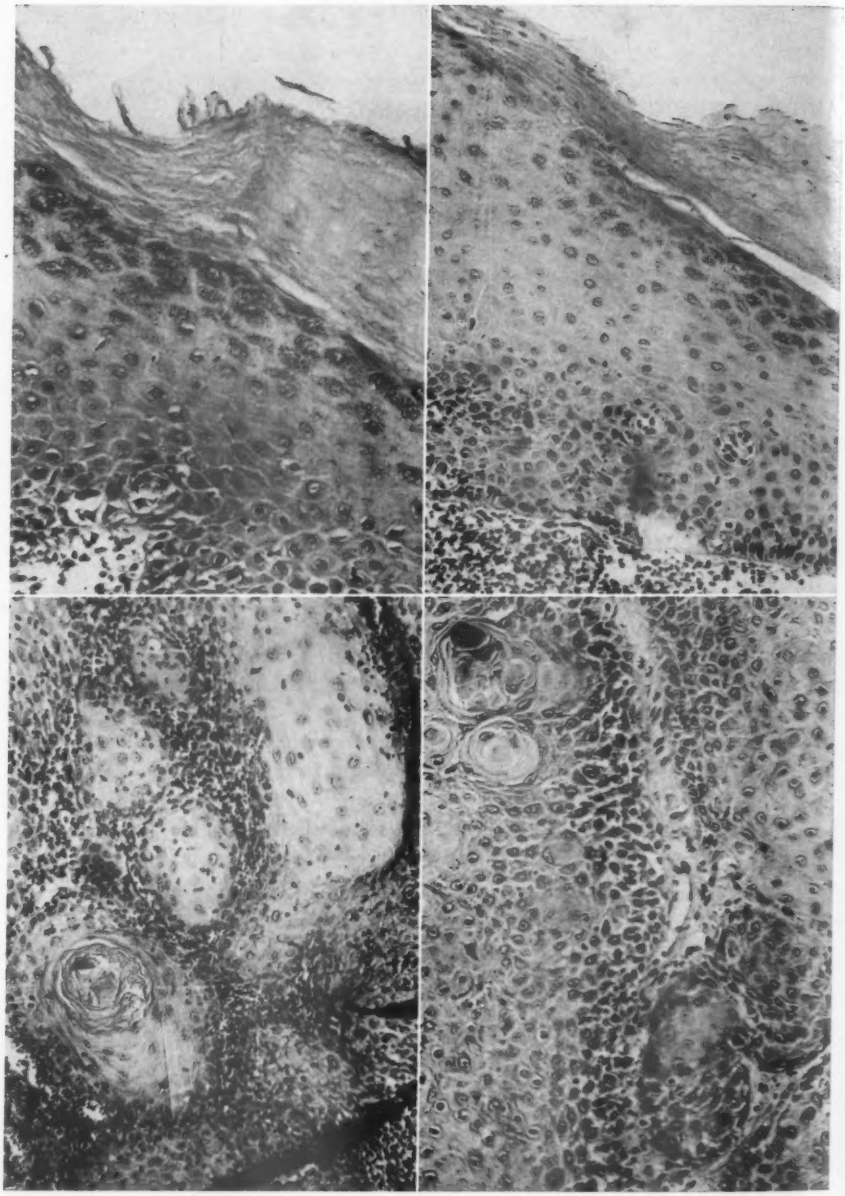

Fig. 3.

Fig. 4.

(For legends, see opposite page.)

was no complaint at this time, and the oral examination was carried out as a routine procedure.

The examination revealed that an area measuring 1.5 cm. in its greatest diameter was located on the left buccal mucosa and gutter in the second mandibular molar region. A biopsy was performed, and the pathologist's report indicated "benign hyperplasia and hyperkeratosis." The patient was advised to return in six months and to stop the use of snuff.

Fig. 5.—Section taken six years after the first biopsy now shows epidermoid carcinoma and invasion. The patient received surgical treatment, with neck dissection.

The patient returned one year after this initial examination and stated that she had not discontinued the use of snuff. The area was again biopsied, and the pathologist's report revealed "hyperkeratosis with parakeratosis." The patient was given a treatment plan and advised to return in six months.

On the patient's third visit to the clinic, the lesion showed gross changes and was again biopsied. Microscopic examination revealed hyperkeratosis, acanthosis, and verrucous hyperplasia. The patient was advised to have the area removed surgically, but she did not return for this treatment.

On the fourth visit, four years after the patient was first seen, another biopsy was taken and demonstrated dyskeratosis with a definite malignant pattern. The patient again refused treatment.

Fig. 1.—Section from the buccal mucosa showing hyperkeratosis. This section was obtained in 1951 and was from an area in which snuff had been held frequently over a period of twenty-five years.

Fig. 2.—Section taken in 1952, one year later than the section shown in Fig. 1. There is hyperkeratosis, parakeratosis, and some unusual cellular activity in the basal layers.

Fig. 3.—Section obtained in 1953, about one year after the section shown in Fig. 2. Note verrucous hyperplasia, as well as unusual cellular activity.

Fig. 4.—Section obtained four years after the original section shown in Fig. 1. This section, which was removed from the same lesion, shows dyskeratosis with a malignant pattern.

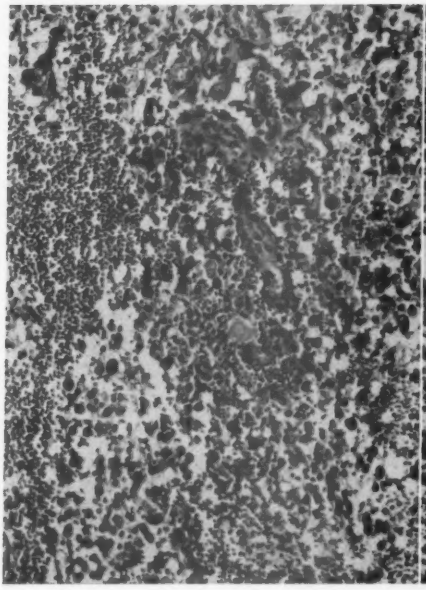

Fig. 6.

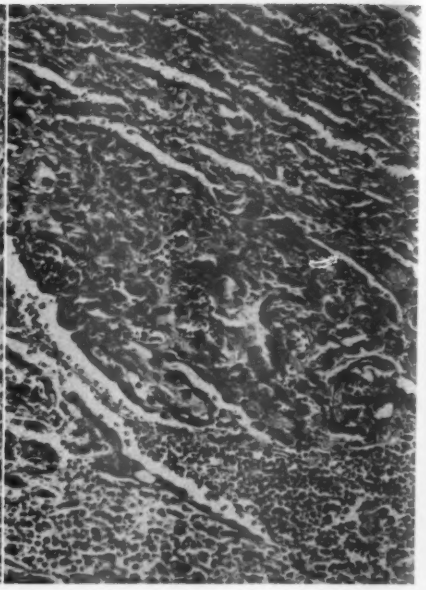

Fig. 7.

Figs. 6 and 7.—Sections taken from the lung eighteen months after the mouth surgery show metastatic spread of the malignant involvement from the buccal mucosa.

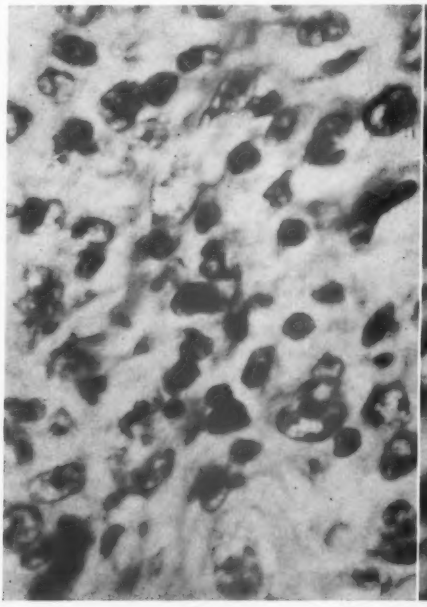

Fig. 8.

Fig. 9.

Fig. 8.—Enlargement of the malignant growth from the buccal mucosa and floor of the mouth.

Fig. 9.—Enlargement of the malignant growth from the lung.

Six years following the initial examination the patient demonstrated epidermoid carcinoma of the buccal mucosa, with extension to the floor of the mouth and palpable nodes in the left cervical chain. She submitted to a mandibular resection and left neck dissection.

Six months after the operation a small suspicious area was noted in the floor of the mouth and biopsied. This proved to be epidermoid carcinoma and was thought to be residual disease.

Eighteen months following the operation the patient complained of vague chest pain and a nonproductive cough. Examination revealed a 2 cm. mass in the left lung. This was biopsied and diagnosed as anaplastic epidermoid carcinoma, which was thought to be a metastatic tumor from the primary oral region.

CONCLUSION

This unfortunate case demonstrated two very important points: (1) that we may be able to follow histologically the transformation of a benign lesion into a malignant lesion, and (2) the importance of early diagnosis and treatment of lesions that may develop into malignant tumors.

If the patient had been treated early in the course of the disease, before irreversible changes had occurred, the end result might possibly have been avoided.

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ENDODONTICS

The American Association of Endodontists

Captain Warren J. Hedman, Editor

THE EFFECT OF TEMPERATURE CHANGE ON THE SEALING PROPERTIES OF TEMPORARY FILLING MATERIALS

Part I

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*Peter Kapsimalis, M.S., D.D.S.,** Summit, N. J.*

ONE of the prime considerations in the selection of a temporary filling material is the material's ability to seal the margins of the cavity within which it is placed. Temporary filling materials are used in many phases of dentistry. During restorative dental procedures, temporary filling materials are used to protect the prepared tooth surface until the final restoration is placed. During endodontic procedures, temporary filling materials are used to seal the access opening in the crown between treatments so as to prevent fluid exchange between the root canal and the mouth.

The authors of current endodontic textbooks all agree on the importance of sealing the access opening between treatments, but they do not agree on the material to be used.

Grossman,[1] in discussing the selection of a temporary filling material, states that zinc oxide-eugenol cements are probably the best and that gutta-percha preparations, intermediate, and zinc phosphate cements are the worst. He recommends the use of zinc phosphate cement placed over gutta-percha to seal posterior teeth. For anterior teeth, he recommends zinc oxide-eugenol cement over gutta-percha.

Presented at the annual meeting of the American Association of Endodontists, Chicago, Illinois, Feb. 6, 1960.

This research report is the first phase of a broad study to determine the relative efficiency of sealing agents utilized in dentistry.

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Sommer, Ostrander, and Crowley[2] state that the pulp-chamber opening should be sealed by applying a softened layer of gutta-percha over the dressing, with a space of 1.5 mm. allowed for the final cement seal. The operator is cautioned that "gutta-percha is not a leakproof seal. Therefore, if any should adhere to the side of the pulp chamber it would afford avenues of leakage and result in contaminated cultures." The pulp chamber opening is then dried with alcohol, and the orifice is sealed with a creamy mix of "permanent cement."

Stewart[3] mentions that a double seal is generally employed to prevent medication from escaping from the tooth; the inner seal generally consists of gutta-percha, and an outer seal of "some cement substance is then placed."

Coolidge and Kesel[4] merely state: "The tooth is sealed up with cement until a subsequent appointment."

It is obvious from the foregoing that a controlled study was indicated to determine which material would most effectively seal the coronal access opening between endodontic treatments so as to prevent fluid exchange between the root canal and the mouth.

PREVIOUS STUDIES

Room Temperature.—In 1939, Grossman[5] investigated the sealing properties of temporary filling materials. As a testing procedure, he used glass capillary tubes, the inner surface of which had been roughened with a coarse carborundum stone. Each tube was filled at one end with the test filling material to a depth of 2 or 3 mm. The portion of the tube above the test filling material was packed with a cotton wick. Tubes so prepared were suspended over an aqueous solution of dye, the filled end was submerged, and the unfilled open end extended above the level of the dye. Discoloration of the cotton wick by the dye solution indicated leakage of the test filling material. Grossman found the sealing properties of the zinc phosphate cements the worst, the gutta-percha fillings intermediate, and the zinc oxide-eugenol cements the best.

He states: "Zinc oxide-eugenol cements were found to be leakproof, without exception, in all cases."

Fischer[6] made a careful study of the sealing properties of zinc phosphate cement and other, permanent, filling materials. He found that under the conditions of testing used in his study, every filling material tested showed some degree of fluid penetration at the margin.

Massler and Ostrovsky,[7] and Weiss[8] tested the relative sealing properties of a number of commonly used filling materials. The results of these two studies confirmed the reports of previous investigators, that is, that the commonly used filling materials exhibit marginal leakage in a relatively short period of time and that, at room temperature, zinc oxide-eugenol cement and amalgam are the most effective sealing agents.

Temperature Change.—In 1952, Nelson, Wolcott, and Paffenbarger[9] demonstrated the effect of temperature change on the marginal seal of various, filling materials. They determined that a temperature change of 43° C. was produced

under an acrylic restoration when test subjects drank beverages adjusted to the upper and lower limits of thermal tolerance of the mouth (60° C. and 4° C., respectively). Taking into consideration this temperature change and the difference in the coefficients of thermal expansion of the resin filling and tooth structure, they computed that a crevice 10 microns in diameter could develop at the junction of the filling and the tooth surface during the cooling cycle. Although this crevice is below the limit of visual acuity, which is 50 microns, it is five to twenty times as large as the size of bacteria commonly found in the mouth (for example, lactobacillus, 2 microns; streptococcus, 0.5 microns).

In 1955 Seltzer[10] tested the penetration of color-producing microorganisms through the margins of acrylic and amalgam restorations, both at constant body temperature and after various temperature changes. In no instance did the organisms penetrate the margins of the restorations maintained at constant body temperature. Penetration of microorganisms did take place, however, in teeth that had undergone temperature change.

In 1958 Hirsch and Weinreb[11] investigated the cavity-sealing properties of silicate cements, acrylic filling materials, and amalgam under conditions simulating those found in the mouth. They reported that although acrylic restorations exhibit a very satisfactory initial cavity seal, after repeated temperature changes a solution of a dye was able to penetrate between the tooth and the acrylic filling material. This penetration was attributed to the difference in thermal expansion between the tooth and the acrylic restoration. The marginal adaptation of silicate cements was unsatisfactory before and after repeated temperature change. Of the materials tested, only amalgam maintained its good marginal seal after repeated temperature change.

It was apparent, after a review of the literature, that the sealing properties of temporary filling materials had not been evaluated under conditions similar to those encountered in the mouth. The following experiments were therefore performed, our objective being to test the sealing properties of temporary filling materials by means of test procedures that produced as closely as possible conditions similar to those found in the mouth.

TEST PROCEDURE

Tooth Preparation.—One hundred seventeen recently extracted noncarious, nonrestored, sound anterior teeth were used in this study. During the time between extraction and the laboratory procedures, an interval which was kept minimal, the teeth were stored in normal saline solution to prevent desiccation.

Approximately 2 mm. of the root end of each tooth was removed with a carborundum disc. A Class 1 type of cavity was prepared in the center of the cut root end and filled with amalgam. This was done to eliminate the possibility of dye penetration through the root apex area (Fig. 1).

On the lingual surface, halfway between the incisal edge and the cingulum, a funnel-shaped access cavity was prepared, exposing the pulp chamber. This cavity was of a size and shape that would permit convenient endodontic manipulation. The material in the pulp chamber was removed with a No. 6

round bur. No attempt was made to remove material in the root canal, since it was felt that any such material would be an added barrier to seepage from the root apex area.

Cotton fibers were packed into the clean, dry pulp chamber to a level approximately 2 mm. below the lingual surface of the funnel-shaped access cavity. The filling material to be tested was placed over the cotton fibers until the access cavity was filled. All materials used were burnished tightly against the margins of the cavity to ensure as perfect a marginal adaptation as possible.

MATERIALS

Nine filling materials were included in this study—eight commonly used temporary filling materials and amalgam, which was included as a control. Tested were gutta-percha (both temporary stopping and base plate), two brands of zinc phosphate temporary cement, two brands of zinc phosphate permanent cement, zinc oxide-eugenol cement, Cavit (a zinc oxide, polyvinyl preparation), and amalgam.

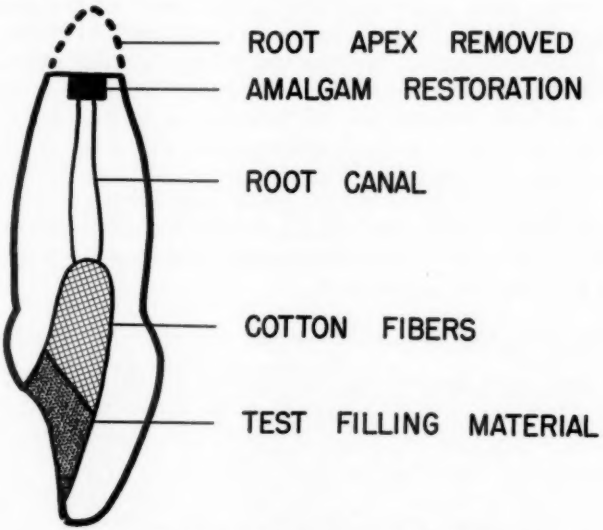

Fig. 1.—Diagrammatic cross section of test tooth.

The cavity-sealing properties of all test materials were evaluated both at room temperature and after being subjected to repeated temperature change.

Manipulation of Materials.—Gutta-percha materials were warmed gently and placed within the access cavity while soft. As it cooled, the gutta-percha was burnished against the cavity walls with a ball burnisher. The zinc phosphate temporary cements and the zinc phosphate permanent cements were mixed on a glass slab in the proportions recommended by each manufacturer until the consistency was that of heavy cream. The cement was then placed within the access cavity, and as the cement hardened it was burnished against

the cavity margins. The zinc oxide-eugenol cement was mixed to a puttylike consistency immediately before use. The excess eugenol was expressed by squeezing the mass between the folds of an amalgam squeeze-cloth. The zinc oxide-eugenol mixture was then placed within the cavity. The excess was removed by wiping the lingual surface of the tooth with a cotton pellet dampened with water. The material was at the same time burnished against the cavity margins with the dampened cotton pellet. The Cavit was squeezed from its tube and placed within the access cavity. It was manipulated in a manner similar to that used with the zinc oxide-eugenol cement. The amalgam restorations were placed by accepted operative techniques.

After the test filling was placed within the access cavity, the tooth was returned to the normal saline solution. The prepared and filled teeth were stored in saline solution at room temperature for twenty-four hours before testing, to permit the restorations to "mature."

ROOM TEMPERATURE STUDY

Twenty-seven teeth were included in this phase of the study. After storage in normal saline solution at room temperature for twenty-four hours, three teeth filled with each of the nine test filling materials were placed in a 2 per cent aqueous solution of aniline blue dye. The teeth remained in the dye solution at room temperature for seventy-two hours. They were then removed from the solution, washed, and scrubbed with a brush to remove all traces of dye from the surface. The teeth were sectioned longitudinally to expose the cotton fibers in the pulp chamber under the test filling material. A blue discoloration of the cotton fibers indicated an imperfectly sealed access cavity. If the color of the cotton fibers remained unchanged, it indicated that a leak-proof seal had been maintained.

TEMPERATURE-CHANGE STUDY

Ninety teeth were included in this phase of the study. After storage in normal saline solution at room temperature for twenty-four hours, ten teeth filled with each of the nine test filling materials were placed in water at 60° C. for one minute and then transferred to a 2 per cent aqueous solution of aniline blue dye at 4° C. for one minute. This was then repeated nine times, making a total of ten temperature cycles. The teeth were removed from the solution, washed, scrubbed with a brush to remove all traces of the dye from the surface, and sectioned longitudinally as above.

RESULTS

Room Temperature Study.—After immersion in the dye solution at room temperature for seventy-two hours, all teeth filled with the following materials showed definite leakage of dye into the pulp chamber: temporary stopping gutta-percha, base plate gutta-percha, both brands of zinc phosphate temporary cement, and both brands of zinc phosphate permanent cement. Dye penetration was along the junction of the filling material and tooth structure.

None of the teeth filled with zinc oxide-eugenol cement, Cavit, or amalgam showed leakage of dye into the pulp chamber.

Temperature Change.—In teeth subjected to ten cycles of temperature change from 60° C. to 4° C., the following results were obtained: All teeth filled with the following materials evidenced definite leakage of dye into the pulp chamber: temporary stopping gutta-percha, base plate gutta-percha, both brands of zinc phosphate temporary cement, and both brands of zinc phosphate permanent cement. Five out of ten teeth filled with zinc oxide-eugenol cement showed leakage. Cavit did not allow dye penetration in any of the ten teeth filled with this material. Amalgam was equally effective in its ability to maintain a leakproof seal (Fig. 2).

FILLING MATERIAL		ROOM TEMPERATURE—72 HRS.		TEMPERATURE CHANGE 60° C.—4° C. (10 CYCLES)	
		NO. OF TEETH	LEAKAGE	NO. OF TEETH	LEAKAGE
Gutta-percha temporary stopping	(Caulk)	3	3	10	10
Gutta-percha base plate	(Caulk)	3	3	10	10
Zinc phosphate temporary cement	(Moyer)	3	3	10	10
Zinc phosphate temporary cement	"Pro-tem" (Caulk)	3	3	10	10
Zinc phosphate permanent cement	(Flecks)	3	3	10	10
Zinc phosphate permanent cement	(Ames)	3	3	10	10
Zinc oxide-eugenol	(U. S. P.)	3	0	10	5
Cavit	(Premier)	3	0	10	0
Amalgam	(S. S. White)	3	0	10	0

Fig. 2.—Results of room temperature and temperature-change study.

DISCUSSION

The conditions under which this study was conducted may appear more exacting than necessary, since the materials were to be evaluated under conditions reproducing as closely as possible conditions of clinical usage. Nevertheless, we decided to use a dilute aqueous solution of dye rather than a saliva-dye suspension, since the oral environment is often aqueous in nature. This is especially true during the ingestion of beverages (which are often at the extremes of the mouth's thermal tolerance) and during oral hygiene procedures (which often involve compounds, one of whose ingredients may be a surface-tension-reducing agent). The use of such preparations would markedly alter the normally viscous nature of fluids in contact with tooth surfaces.

Cavities prepared in recently extracted teeth were used, rather than cavities prepared in laboratory apparatus. It was felt that this would more nearly parallel conditions of clinical usage.

Teeth filled with the test materials were immersed in the dye solution during the cooling phase. Souder and Paffenbarger[12] and Nelson and co-workers[9] showed that the space at the junction of the tooth wall and the filling material is widest during the cooling cycle.

Three teeth filled with each of the test filling materials were included in the study under conditions of room temperature, since this phase of the investigation was conducted to explore work reported by previous investigators.[5-8]

The results obtained in the temperature-change phase of the study were not unexpected, for the most part. It was not surprising to find that materials which permitted dye penetration at room temperature also sealed cavities poorly when subjected to ten cycles of temperature change. It was surprising, however, to find that the zinc oxide-eugenol cement, which up to the present had been considered the most effective cavity-sealing agent (on the basis of previous studies conducted at room temperature), did not seal cavities as well as might be expected. Zinc oxide-eugenol cement sealed only five of the ten test cavities in which it was used when teeth so filled were subjected to ten cycles of temperature change. The only temporary filling material which effectively sealed all experimental cavities, under conditions of this study, was Cavit. Amalgam, a permanent filling material, was equally effective.

SUMMARY

The cavity-sealing properties of nine filling materials (eight temporary filling materials and amalgam) were tested at room temperature and also after ten cycles of temperature change from 60° C. to 4° C. The ability of a 2 per cent aqueous solution of aniline blue dye to penetrate the margins of cavities filled with each of the test filling materials was used as a means of comparing their cavity-sealing properties. The inability of the test filling material to maintain a leakproof seal of the cavity margins was evidenced by a blue discoloration of cotton fibers placed beneath the test filling.

Under the conditions of testing at room temperature, the following materials showed consistent leakage: temporary stopping gutta-percha, base plate gutta-percha, two brands of zinc phosphate temporary cement, and two brands of zinc phosphate permanent cement. The materials that showed no leakage at room temperature were zinc oxide-eugenol cement, Cavit, and amalgam.

Of the teeth similarly filled with each of the nine test filling materials and subjected to ten cycles of temperature change, those which showed leakage to the dye solution at room temperature also showed leakage when subjected to temperature changes. Although zinc oxide-eugenol cement did not show leakage at room temperature, it did show leakage in five out of ten teeth subjected to temperature changes.

Of the temporary filling materials tested, only Cavit maintained a leakproof cavity seal both at room temperature and after repeated temperature changes.

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SECOND INTERNATIONAL CONFERENCE ON ENDODONTICS

THE following reports were agreed upon by the group leaders of the Second International Conference on Endodontics. In view of the fact that they are of general interest to those practicing endodontics, they are published here to give the deliberations of the Conference greater currency. Some of the statements may appear to be elementary when removed from context. The reader may refer to the papers presented at the Conference in the *Transactions of the Second International Conference on Endodontics*, issued by the Postgraduate Office of the School of Dentistry, University of Pennsylvania, Philadelphia, Pennsylvania.

SUMMARY OF REPORTS

1. The function of the pulp is both formative and reparative.

2. The large young pulp is rich in cellular material by which it is capable of defending itself from external insult. The smaller adult pulp, though less rich in cellular material, is partially protected by a thicker wall of dentine.

3. A properly treated pulpless tooth does not interfere with the integrity of the attachment apparatus.

4. Pulp damage can occur from injudicious operative techniques at any speed. Special precautions with respect to cooling mechanisms must be exercised, especially when high-speed techniques are used.

5. Obturation of the root canal is best achieved by means of a nonabsorbable material in conjunction with a solid core, such as gutta-percha, silver cone, etc.

6. Pulp stones have been observed histologically in about 75 per cent of cases, and they are therefore without clinical significance when observed roentgenologically.

7. There is no clinical evidence that accessory canals are of significance if the main root canal is well filled. Additional histologic research should be done to determine what happens to accessory canals following root canal treatment.

8. There is a possibility that, in rare cases, bruxism may cause death of the pulp.

9. Cultures should be made before a root canal is filled, as the culture method is the most effective way to determine the presence of microorganisms. It was the consensus of the conferees that such a procedure increases the probability of success.

10. Endodontic treatment is not altogether one of bacterial disease but involves basic principles of eliminating the environment in which viable and nonviable irritants may exist.

11. Where positive cultures persist, leakage should be suspected.

12. Instrumentation beyond the confines of the root canal should be avoided in order to prevent the possibility of causing a bacteremia and/or periapical irritation.

13. While present culture media appear to be reasonably adequate, research studies leading to the development of more sensitive culture media should be encouraged.

14. There is no correlation between clinical symptoms and types of organisms isolated from root canals.

15. In case of sensitivity to an antibiotic, that antibiotic should be avoided.

16. Antibiotics or sulfonamides should be used prophylactically when there is a history of rheumatic or congenital heart disease or any diseased state that might become aggravated by a transient bacteremia.

17. Indiscriminate use of antibiotics or corticosteroids is to be condemned, but their judicious use is acceptable.

18. The effectiveness of combinations of antibiotics or combinations of antibiotics with other agents for root canal sterilization has been established.

19. A number of nonspecific germicidal agents have proved to be effective for root canal sterilization.

20. A fistula requires no special treatment, as it will heal when the canal is rendered sterile.

21. "There is a greater chance of dissemination of microorganisms from an infected vital pulp where the bacteria are in direct contact with the blood stream than from a granuloma where the defensive mechanisms are marshalled to overwhelm and isolate any wandering bacteria and their toxic products." This statement was reiterated (*Transactions of the World Conference on Endodontics*, Philadelphia, 1953, Stephenson Brothers, p. 104).

22. Further studies in improved methods of diagnosis leading to pulp conservation are needed.

23. In cases of incomplete resolution of an area of rarefaction with a seemingly well-filled root canal, preoperative and follow-up roentgenograms should be compared.

24. The cleansing and enlarging of the root canal by instrumentation and irrigation are more important to success in endodontic treatment than the use of any particular form of medication. The addition of an acceptable germicidal agent may be considered to increase the probability of disinfection of the canal.

25. Existing methods of pulp testing are not infallible, especially in recently erupted permanent teeth, following traumatic injury to the teeth, or where there is extensive deposition of secondary dentine. Periodic examination is recommended in such cases.

26. In an acute alveolar abscess, drainage should be established.

27. Roentgenograms should be used not only for diagnosis but as a guide in root canal treatment and filling.

28. The principles of endodontic treatment were agreed upon with these exceptions: (a) omit principle No. 3; (b) in principle No. 9, omit the word "hermetic" and add "further, provided that it is insoluble and impermeable." (The principles are appended.)

29. In cases of leukemia, exposure to intensive radiation, and other severe diseases, root canal treatment rather than any form of surgery should be carried out.

30. A perforation which can be sealed off is not a contraindication to root canal treatment.

31. In cases of root resorption, root canal treatment may be attempted, followed by a period of observation.

32. Standardization of root canal instruments and materials is urged, and the recommendation was made that additional work in this regard be continued.

33. Root canal filling materials should conform to the sizes and tapers of root canal instruments.

34. Studies should be encouraged to develop a simpler and more certain means of obturating the root canal.

35. A physiologic root canal filling material which would bring about sealing of the apical foramen by cementum would be most desirable.

36. Endodontic treatment of teeth in which there is discharge through the gingival crevice may be attempted, provided a diagnostic exploratory procedure indicates a favorable prognosis for the periodontal membrane.

37. The prognosis for endodontic treatment compares favorably with other dental operations performed.

PRINCIPLES

Principle No. 1: An aseptic technique should be followed in all cases of root canal treatment.

Principle No. 2: Instruments should be confined to the root canal, so as not to injure periapical tissue.

Principle No. 3: A root canal should first be entered by a fine, smooth canal instrument to minimize the possibility of forcing infected debris through the apical foramen.

Principle No. 4: In practically all cases the root canal needs to be enlarged, even though it may be fairly wide already.

Principle No. 5: The root canal should be flooded with an antiseptic solution during instrumentation.

Principle No. 6: The antimicrobial agent used for sterilizing the root canal should be nonirritating to the periapical tissues.

Principle No. 7: A fistula requires no special treatment.

Principle No. 8: In all cases of root canal treatment, a negative culture should be obtained before filling the root canal.

Principle No. 9: The method of filling a root canal is immaterial, provided a hermetic seal is obtained.

Principle No. 10: The root canal filling should be acceptable to the periapical tissue.

Principle No. 11: In the case of an acute alveolar abscess, drainage must be established for an adequate length of time.

Principle No. 12: An incision should be made only when the swelling is soft and fluctuant.

Principle No. 13: An injection into an infected area should not be made, whether it be a local anesthetic alone or a combination of a local anesthetic with penicillin.

Principle No. 14: Not all pulpless teeth are amenable to treatment, nor are all patients candidates for endodontic service.

STUDIES IN DIAGNOSIS IN ORAL SURGERY AND ORAL MEDICINE

Lester R. Cahn and Kurt H. Thoma

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EXFOLIATIVE CYTOLOGY FOR DETECTION OF EARLY MOUTH CANCER

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More than 100 years have elapsed since Hermann Lebert[1] proposed that characteristics of cells from cancer lesions provided a basis for diagnosis. Since then, the classical studies of Papanicolaou[2] and the contributions of many other investigators[3-6] have demonstrated that cytology is both useful and reliable in the diagnosis of cancer. The effective application of cytologic methods to the detection of asymptomatic uterine cancer, as well as to the diagnosis of early cancer in other areas of the body, suggested that cytologic methods might be equally effective in the detection of minimal asymptomatic oral carcinoma. Although the medical literature contains few references to the cytology of oral mucosa,[7-9] it was known that scrapings from the surface of clinically recognizable oral cancer can yield aberrant cells suggestive of carcinoma.[10-13]

In the present investigation, the following questions were explored: (1) How reliable is cytologic examination as a diagnostic technique? (2) Will cytologic examination disclose cancer in lesions which are so inconspicuous that neoplasia is not suspected?

OUTLINE OF STUDY

Dental services in Veterans Administration hospitals are charged with the responsibility of oral examination as an integral part of the over-all physical

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examination given all patients. The soft and hard structures of the mouth are carefully examined, and any abnormalities are recorded. When indicated, treatment is provided for acute and benign oral conditions as part of dental care.

In the three-year period, from 1956 to 1959, oral examinations were completed for 16,103 patients at the VA Hospital in Brooklyn, New York. All abnormalities of the oral or oropharyngeal mucosa were selected for cytologic study, regardless of how insignificant the lesion or how obvious the clinical diagnosis. There were 412 patients who presented with 452 abnormalities of the oral mucosa. Scrapings for cytologic examination were taken from each abnormality, and biopsies were performed whenever warranted by clinical or cytologic evidence.

TABLE I. ABNORMALITIES OF THE ORAL MUCOSA DETECTED AMONG 16,103 PATIENTS

Total patients examined	16,103
Total oral abnormalities scraped for cytology	452
No justification for biopsy	213
Smear and biopsy available	239

It was assumed a priori that the histopathology of a tissue specimen was the most stable basis for diagnosis of carcinoma, so that the reliability of the cytologic diagnosis was assayed against the histopathologic findings. There was no clinical or cytologic justification for biopsy in 213 lesions, however, so only a smear was obtained in these cases. The remaining 239 oral lesions were excised or a specimen was taken for biopsy after the surface had been scraped for cytologic examination, and these constitute the sample described in this report (Table I).

METHOD

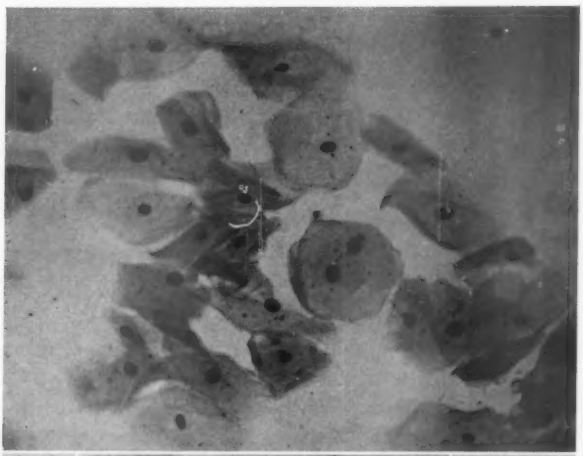
The entire surface of the abnormal mucosa was firmly scraped with the edge of a wooden tongue depressor. The material thus removed was spread directly on a previously identified microscopic slide and immediately fixed in 95 per cent alcohol. The slides were then stained by a modified Papanicolaou stain.

White lesions which usually suggest a keratin surface were scraped until the white surface was partially removed in order to make the underlying cells accessible. If this was not feasible, any cracks or fissures were spread open for deeper access. Debris, blood, and slough were removed by wiping the surface of the lesion prior to scraping. Fresh blood did not seriously impede the staining or reading of the sample, provided that the surface of the lesion was wet and the smears were not permitted to dry.

The cytologic findings were independently determined and recorded several days before the histologic reports became available. Smears were interpreted by one person (H. C. S.) and reviewed by another (S. S. S.). When differences of opinion arose, they were discussed and a cytologic classification was agreed

upon. Tissue specimens of the oral lesions were routinely processed and reported by the Pathology Section of the hospital, and they were subsequently reviewed by the oral pathology consultant (L. R. C.).

Fig. 1.



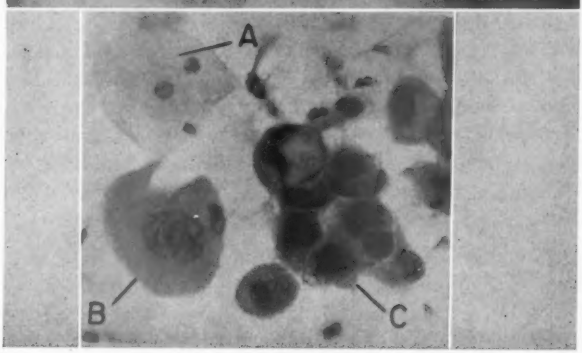


Fig. 2.

Fig. 1.—Precornified cells from normal buccal mucosa. The cells are clearly defined and relatively flat, with irregular outline and granular inclusions. The ratio of nucleus to cytoplasm varies from approximately 1:10 to 1:100. The color of the cytoplasm changes with maturation from pale blue (parabasal cells) to light pink (precornified cells) to orange (cornified cells), and the nucleus becomes more pyknotic until it disappears. (Papanicolaou's stain. Magnification, ×400.)

Fig. 2.—Photomicrograph of scraping from an ulcer of the floor of the mouth, adjacent to the border of the lower denture. *A*, Normal epithelial cells. *B*, Binucleate cell with enlarged, granular nuclei. *C*, Cluster of cells with poorly defined borders, vacuolated cytoplasm, enlarged, hyperchromatic nuclei of irregular outline, and variable size. Histologic diagnosis: squamous-cell carcinoma. (Papanicolaou's stain. Magnification, ×400.)

FINDINGS

Normal epithelial cells observed in smears were classified, according to degree of maturity, as basal, precornified, and cornified cells. Parabasal cells usually stained blue-green, with evenly granular nuclei and relatively small

nucleoli. Precornified squamous cells were flatter, polyhedral, and irregular in shape; they had smaller, denser nuceli, and the nucleocytoplasmic ratio varied from about 1:6 to 1:50 or more. Cornifying cells stained more pink to red-orange, and the nuclei were more pyknotic. Anuclear keratinized cells were also commonly observed (Fig. 1).

Fig. 3.

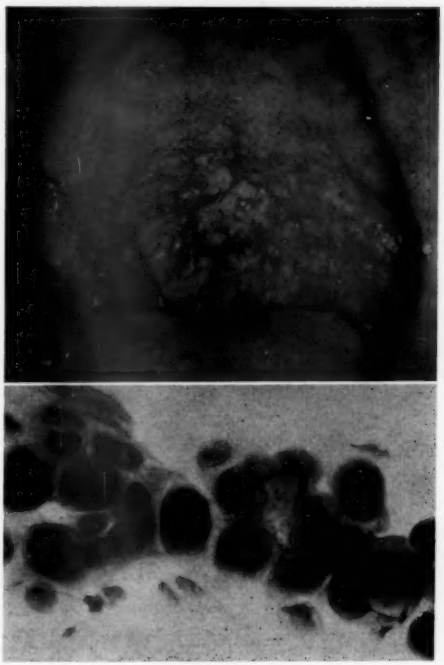


Fig. 4.

Fig. 3.—Obvious primary carcinoma of the soft palate.

Fig. 4.—Photomicrograph of scraping from the surface of the lesion shown in Fig. 3. The cells tend to be round, ovoid, and spherical and are densely packed. Their cytoplasm is orangeophilic. The nuclei are hyperchromatic and vary widely in size and shape, with chromatin condensed into strands and clumps. There is some abnormal multinucleation, and the nucleocytoplasmic ratio is on the order of 1:3 to 1:5. (Papanicolaou's stain. Magnification, ×400.)

Smears derived from carcinomas contained, in addition to many normal cells, recognizable aberrant epithelial cells which met one or more of the commonly accepted criteria of malignant cellular changes. In a few instances, the cellular responses to inflammation and radiation produced morphologic characteristics which simulated malignant abnormalities but, for the most part, these cells could be correctly recognized.

Some of the more common cellular abnormalities observed in the smears from oral carcinoma are illustrated in Figs. 2 through 23. The approximate

order of frequency and the significance of aberrant characteristics suggestive of malignancy found on oral smears may be listed as follows:

1. Condensation of nuclear chromatin forming strands, coarse clumps and dense peripheral nuclear outlines.
2. Enlarged nuclei and increased nucleocytoplasmic ratio.
3. Wide variation in nuclear size (anisonucleosis) and shape.
4. Densely packed, hyperchromatic nuclei in compact groups with no visible cellular outlines.
5. Multiple and enlarged nucleoli.
6. Multinucleation with overlapping of enlarged nuclei or polypoid multinucleation.
7. Cytoplasmic orangeophilia with hyperchromatic, misshapen nucleus.
8. Tendency toward spherical shape.
9. Extreme variation in cell size (anisocytosis) and shape.
10. Hyperchromatic, crescentic nucleus peripheral to vacuolated circular zone.

It should be noted that cellular abnormalities were usually multiple in any one smear and not infrequently were found within the same cell.

The reliability of cytology as a diagnostic tool was evaluated in relation to the biopsy diagnosis of carcinoma and analysis of the data disclosed several significant findings.

Of the total of 239 lesions which provided both a smear and a biopsy specimen, 131 disclosed evidence of carcinoma by both techniques. Of these, 124 lesions were visible and clinically suspicious (Table II). Seven cases,

TABLE II. CYTOLOGY AND BIOPSY DIAGNOSIS OF CARCINOMA FROM 239 ORAL LESIONS

DIAGNOSIS			
CYTOLOGY FINDINGS	BIOPSY FINDINGS	CLINICAL APPEARANCE	NUMBER OF CASES
Carcinoma	Carcinoma	Suspect	124
Carcinoma	Carcinoma	Not suspect	7
Not carcinoma	Not carcinoma		88
Not carcinoma	Carcinoma		15
Carcinoma	Not carcinoma		5
Totals			239

however, presented such minimal abnormalities of the oral mucosa that no biopsy was contemplated (see illustrations). It was only because test conditions had increased the "index of suspicion" of the dental staff and the strict interpretation of the protocol that a scraping was taken, and it was only because the cytology was suggestive of carcinoma that the biopsy was considered. In three of these cases a surface erosion of irregular outline with a slight erythema and a faintly granular texture, with no induration, were the only indications of abnormality (Fig. 8). In two cases there was some evidence of thickening

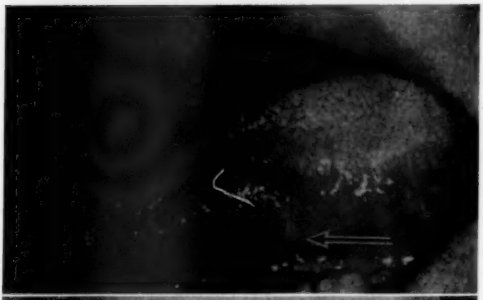
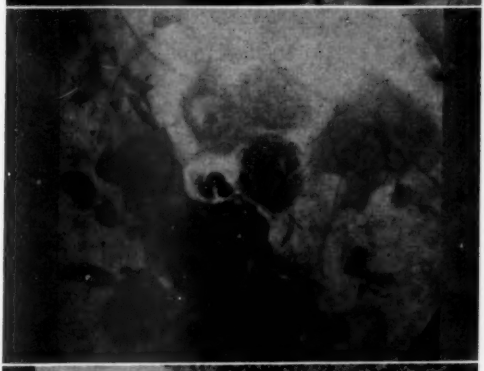


Fig. 5.



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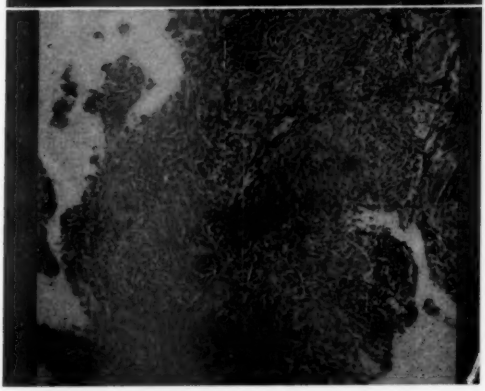

Fig. 7.

Fig. 5.—Asymptomatic lesion of lateral border of the tongue. This lesion, which measures 1 by 1 cm. is raised, with a depressed center, and moderately firm. The mucous membrane is intact. The lesion was detected on routine examination; the patient was unaware of its existence.

Fig. 6.—Photomicrograph of scrapings from surface of lesion shown in Fig. 5. Note cluster of epithelial cells with poorly defined outlines and relatively basophilic cytoplasm, anisonucleosis, and multiple and deeply chromatic nucleoli. (Papanicolaou's stain. Magnification, ×400.)

Fig. 7.—Photomicrograph of biopsy specimen of lesion shown in Fig. 5. Diagnosis: squamous-cell carcinoma. (Magnification, ×100.)

Fig. 8.

Fig. 9.

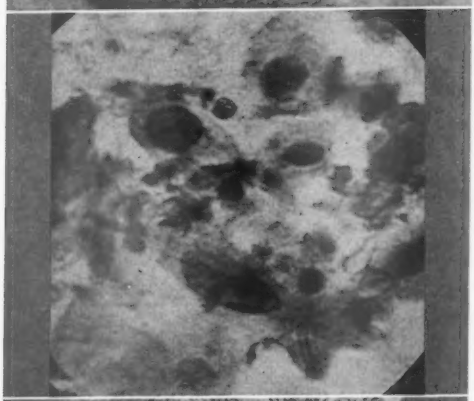

Fig. 10.

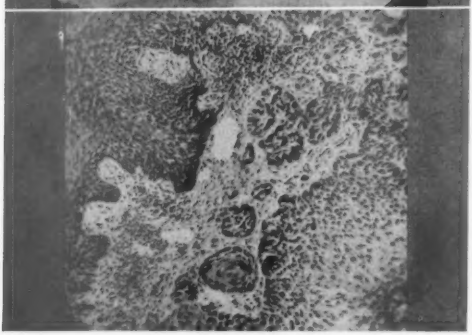

Fig. 8.—Asymptomatic pale surface lesion of the mandibular alveolar process extending irregularly to the anterior pillar. The patient was unaware of this lesion, which was detected on routine examination.

Fig. 9.—Photomicrograph of scrapings from surface of the lesion shown in Fig. 8. Note wide variation in the sizes of cells and nuclei, as well as clumping of nuclear chromatin. (Papanicolaou's stain. Magnification, ×400.)

Fig. 10.—Photomicrograph of biopsy specimen of lesion shown in Fig. 8. Diagnosis: squamous-cell carcinoma. (Magnification, ×100.)

of the surface mucosa and a slightly pale appearance (Fig. 11). In the remaining two cases there was a pale white surface lesion with a faint erythematous outline (Fig. 17).

Fig. 11.

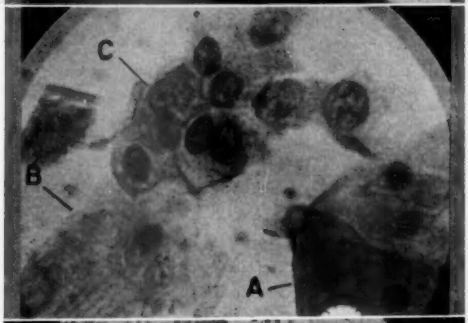

Fig. 12.

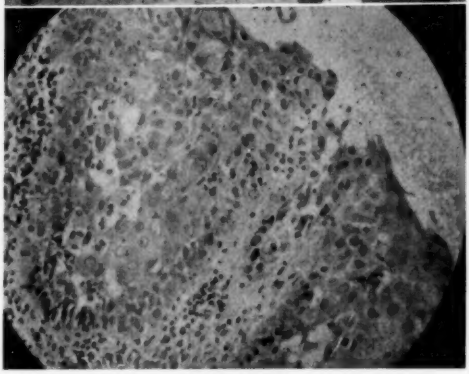

Fig. 13.

Fig. 11.—Asymptomatic pale surface lesion of the soft palate, about 1 cm. in diameter, detected on routine examination; the patient was unaware of the lesion.

Fig. 12.—Photomicrograph of scrapings from the surface of the lesion shown in Fig. 11. *A*, Group of normal epithelial cells. *B*, Enlarged binucleate cell. *C*, Cluster of aberrant epithelial cells with loss of cellular outline, anisonucleosis, multiple, deeply staining nucleoli, and increased nucleocytoplasmic ratio. (Papanicolaou's stain. Magnification, ×400.)

Fig. 13.—Photomicrograph of biopsy specimen of lesion shown in Fig. 11. Diagnosis: intraepithelial carcinoma. (Magnification, ×100.)

Fig. 14.

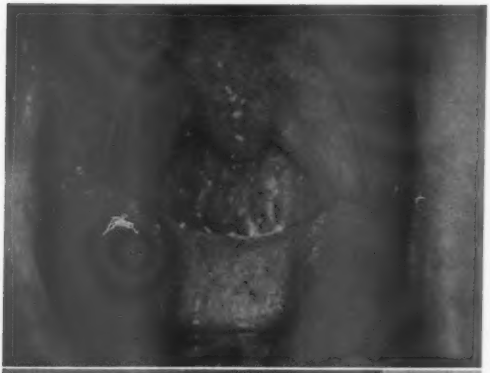

Fig. 15.

Fig. 16.

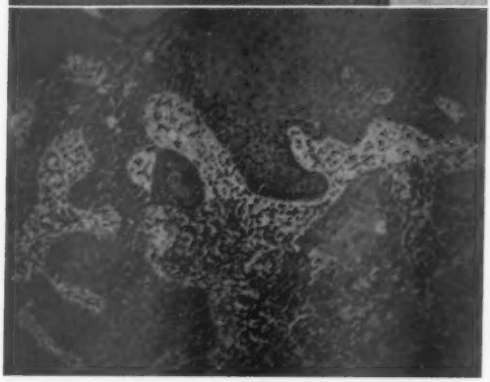

Fig. 14.—Asymptomatic telangiectasia and erythema of the buccal mucosa and hard and soft palate, with several discrete white patches. This lesion was detected on routine examination; the patient was unaware of its existence.

Fig. 15.—Photomicrograph of scraping from the surface mucosa shown in Fig. 14. Note abnormal giant cell with enlarged, hyperchromatic nuclei and multiple nucleoli, increased nucleocytoplasmic ratio, and loss of cellular outline. (Papanicolaou's stain. Magnification, ×400.)

Fig. 16.—Photomicrograph of the second biopsy specimen taken from the junction of the hard and soft palates of the lesion shown in Fig. 14. Diagnosis: squamous-cell carcinoma. The first biopsy of this approximate area was negative. (Magnification, ×100.)

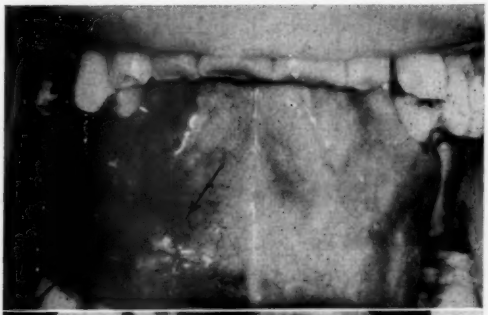

Fig. 17.

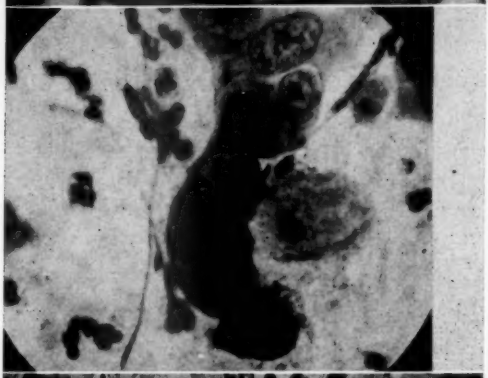

Fig. 18

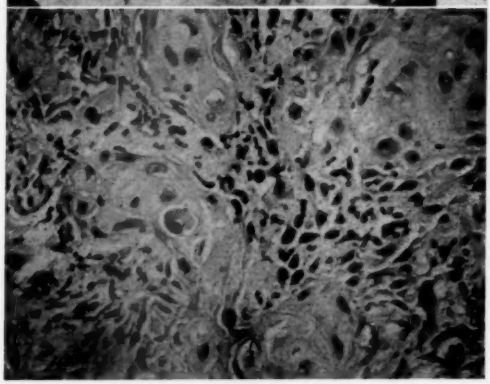

Fig. 19.

Fig. 17.—Asymptomatic, pale, white, superficial lesion of the floor of the mouth, detected on routine examination; the patient was unaware of the lesion's existence.

Fig. 18.—Photomicrograph of scrapings from the surface of the lesion shown in Fig. 17. Note cluster of epithelial cells with enlarged nuclei containing enlarged, deeply chromatic multiple nucleoli. (Papanicolaou's stain. Magnification, ×500.)

Fig. 19.—Photomicrograph of biopsy specimen of lesion shown in Fig. 17. Diagnosis: squamous-cell carcinoma. (Magnification, ×200.)

In seven additional cases more than one biopsy was required to confirm a positive diagnosis obtained by cytologic study. In four of these the second biopsy was positive; in one case three biopsies were required; in one case four

Fig. 20.

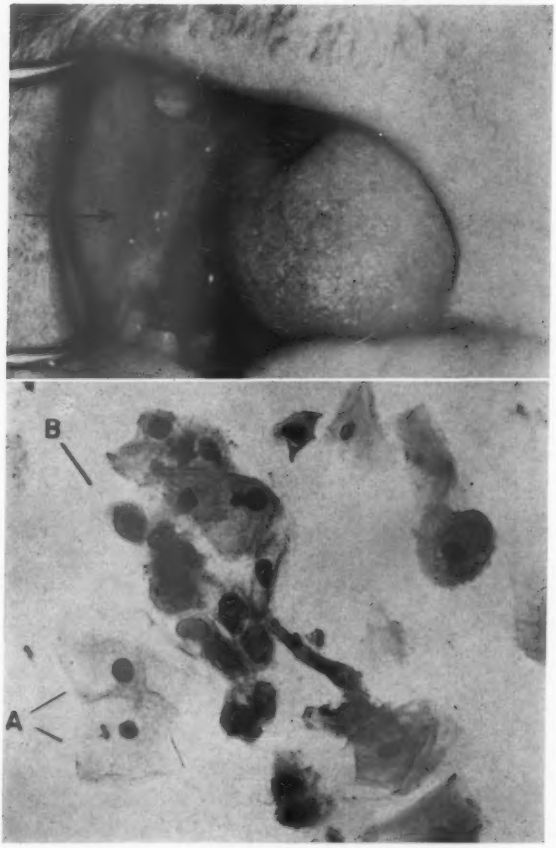

Fig. 21

Fig. 20.—Asymptomatic erythematous surface lesion of the mandibular alveolar process, detected on routine examination; the patient was unaware of the lesion's existence.

Fig. 21.—Photomicrograph of scrapings from the surface of the lesion shown in Fig. 20. *A*, Dyskaryotic epithelial cells with enlarged hyperchromatic nuclei. *B*, Aberrant cells with loss of cellular outline, clumping nuclear chromatin, increased nucleocytoplasmic ratio, anisonucleosis, and irregular nuclear outlines. Confirmed by biopsy. Diagnosis: squamous-cell carcinoma. (Papanicolaou's stain. Magnification, ×400.)

biopsies were taken (all negative) and the diagnosis was confirmed at post-mortem examination; and in one case five biopsies were required before the diagnosis could be confirmed.

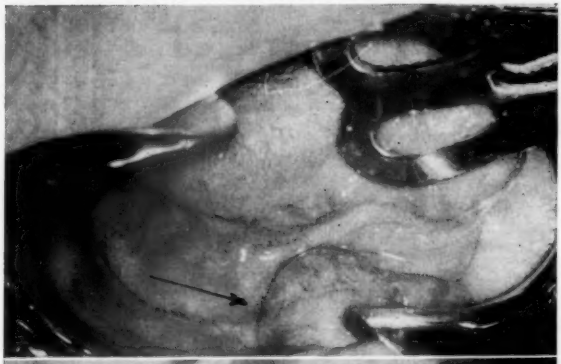

Fig. 22.

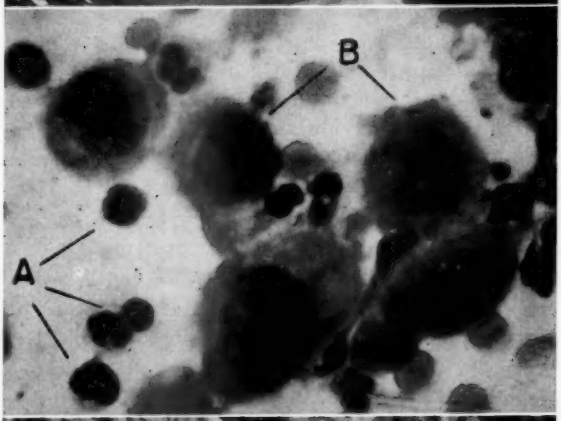

Fig. 23.

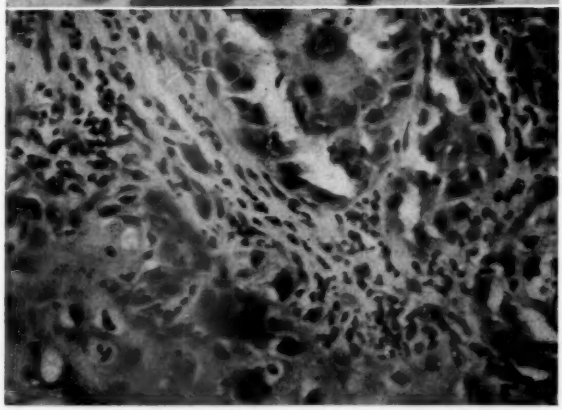

Fig. 24.

Fig. 22.—Swelling, 1 by 1.5 cm., covered by normal-appearing mucous membrane, located on the mandibular alveolar process. The lesion was rubbery to palpation and was first noticed by the patient one month previously when the lower denture did not fit properly.

Fig. 23.—Photomicrograph of scrapings from the surface of the lesion shown in Fig. 22. *A*, Polymorphonuclear leukocytes. *B*, Aberrant epithelial cells with greatly enlarged nuclei, clumping of nuclear chromatin, and a tendency toward ovoid shape. (Magnification, ×600.)

Fig. 24.—Photomicrograph of biopsy specimen of lesion shown in Fig. 22. Diagnosis: squamous-cell carcinoma. (Magnification, ×200.)

The remaining case in this group with positive cytologic and biopsy findings involved a patient who refused biopsy but who consented after the smear revealed carcinoma.

There were eighty-eight oral lesions which were not carcinomatous, as determined by cytologic examination and confirmed by subsequent biopsy.

The twenty cases in which the cytologic and histopathologic findings did not agree were of particular interest. In five cases the smear specimens were considered suggestive of carcinoma, but neither the subsequent biopsies nor clinical observation of the patients have as yet disclosed any evidence of carcinoma. These smears contained cells with unusual morphologic characteristics but, on review, the cytologic findings were of questionable significance. Most of these findings were encountered during the early period of this study, but nevertheless they must be considered as errors in original interpretation.

In the remaining fifteen cases only normal epithelial cells were found on the smear, although subsequent biopsy disclosed carcinoma. One of these was unusual in that, although the biopsy revealed "carcinoma," serial sections of the excised lesion could not provide any further evidence of carcinoma. A review of the original biopsy specimen indicates that the histologic evidence was minimal.

In so far as the detection of cancer of the mouth was concerned, both methods were almost equally reliable. There was over-all agreement between cytologic and histopathologic findings in 219 out of the 239 cases studied (over 91 per cent). (See Table III.) Each was subject to some degree of error, but the correlation between the two methods was high and statistically significant.*

TABLE III. CARCINOMA DIAGNOSIS REVEALED BY CYTOLOGY AND BY BIOPSY

CYTOLOGY FINDINGS	BIOPSY FINDINGS		TOTAL
	CARCINOMA	NOT CARCINOMA	
Positive for carcinoma	131	5	136
Negative for carcinoma	15	88	103
Totals	146	93	239

Pilot study, Aug. 28, 1956, to Oct. 15, 1959.

An incidental finding which arose from this study was the realization that cytology offered an effective method for the follow-up of patients recently treated for head and neck cancer. Postoperatively, these patients often developed granulation tissue, stitch abscesses, delayed wound healing, and draining sinuses. Although these postoperative sequelae were usually of little significance, some were due to a nidus of cancer. Ordinarily these wounds would be observed for some time before they aroused enough suspicion to warrant biopsy, and a superficial biopsy of a sinus tract subsequent to neck dissection may not reveal cancer present in the deeper tissues. Early cytologic detection of recurrence in these cases permitted immediate radiation or surgical therapy.

*The probability of such a relationship occurring by chance is extremely remote. Chi square = 171, $P = < .0001$.

Cancer cells were detected in so many of these unsuspected cases that smears of any unhealed site are now taken routinely after the first few weeks following operation.[14]

DISCUSSION

Notwithstanding modern progress in cancer treatment, early detection of the minimal lesion is the sine qua non of cancer control. While most human cancers originate in such inaccessible anatomic regions that early detection is difficult, early cancer of the mouth should be among the easiest to discover. The mouth's relative accessibility, its frequent inspection, and the acute sensitivity of oral tissues should bring minimal lesions to early attention. Yet, the number of oral cancers that measure less than 1 cm. when first detected is woefully small. This may be attributed to the fact that the early lesion causes no discomfort, is hardly ever noticed by the patient, and is so inconspicuous in its clinical appearance that it is rarely discovered during a cursory examination.

Exfoliative cytology offers the physician and the dentist a practical means of early cancer detection which presents no contraindications, requires minimal equipment, and causes no inconvenience to the patient. Adequate biopsy is undoubtedly the diagnostic procedure of choice, and exfoliative cytology offers no substitute for it. However, this study confirms the fact that cytologic examination performs many valuable diagnostic functions in clinical practice.[14-17]

Perhaps the greatest value of cytologic examination lies in its ability to disclose the presence of intraepithelial or noninvasive oral carcinoma when the clinical appearance is relatively innocent and cancer is not suspected. Its utilization prior to biopsy provides greater assurance of definitive diagnosis, for cancer cells can be detected in the cytologic smear even though the biopsy specimen may be inadequate for diagnosis. The cytologic examination provides a means for the early identification of recurrent carcinoma in the area of primary tumors following treatment of oral malignancies. It can reveal the presence of residual tumors in draining sinus tracts following neck dissection.

SUMMARY AND CONCLUSIONS

Oral examination of 16,103 hospitalized veterans, primarily men over 40 years of age, revealed 452 abnormalities of the oral mucosa in 412 patients. Each abnormality, no matter how insignificant, was scraped for cytologic study. Tissue specimens for biopsy were obtained from 239 of these lesions. The diagnosis of cancer was confirmed independently by both cytologic examination and biopsy in 131 cases. In seven cases, carcinoma was not suspected from the appearance of the lesion, and in an additional seven cases more than one biopsy was required before the diagnosis could be confirmed. Cytologic methods failed in twenty cases.

It was concluded from this study that (1) cytologic examination is a reliable diagnostic procedure for the detection of carcinoma of the mouth; (2) cytologic

study can reveal the presence of early (intraepithelial) oral cancer when the clinical appearance is so innocent that biopsy is not warranted; (3) cytologic examination supplements biopsy, for it can often provide evidence of cancer when the biopsy specimen shows no evidence of malignancy; and (4) cytologic examination simplifies the early detection of recurrence of cancer in treated patients.

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DISCUSSION BY LESTER R. CAHN

When this study was first proposed, I was skeptical. It seemed to me that, since the tissues of the mouth are so visible and so accessible, the information obtained from cytologic examination of a scraping could not be as conclusive as that gained from histologic examination of a portion of tissue. However, when innocuous-appearing spots that had certainly aroused no suspicion revealed unmistakably sinister-looking surface cells which later, on tissue analysis, proved to be malignant, my skepticism changed to amazement.

Florid cancer can be diagnosed clinically. Persistent ulcers are better biopsied and, when small, removed in their entirety. These, however, are not the conditions under discussion here. We are interested in those harmless-looking changes that so often go unnoticed.

Because of the ease with which such superficial lesions can be studied by exfoliative cytology methods, often without the patient knowing that anything is being done, the technique described here is of inestimable value. Widely scattered lesions throughout the mouth, such as those of diffuse white disease,

can be sampled easily from many areas without the patient experiencing the discomfort that would accompany multiple biopsies. Again, the suggestion of a biopsy may cause considerable emotional upset in the cancerophobic patient (and there are many of these), whereas a surreptitious scraping can go a long way toward confirming a diagnosis without unnecessarily alarming the patient.

It is interesting to note that where cytologic examination was positive and the first biopsy was negative, repeated diagnostic procedures confirmed the cytologic diagnosis. This is analogous to the situation in which, although clinical evidence convinces one that a lesion is neoplastic, the first biopsy is negative and then a second biopsy of a specimen taken from a deeper part or a different field, will confirm the clinical impression. If one has faith in the cytologic revelation, he should pursue the search until definite proof is found. This is not always easy to do, as is well illustrated by a case that is not recorded in this article. An enlarged node in the patient's neck proved to be metastatic, but no intraoral, pharyngeal, or nasal lesion was found that would account for it. A scraping from an area of mild erythema of the soft palate on the affected side, however, disclosed definitely malignant cells. Blind biopsies were made to no avail. Shortly before the patient died, a roentgenogram revealed some erosion of the base of the skull, but by that time it was too late for x-ray therapy. At postmortem examination, a lesion high in the pharynx, possibly in Rosenmüller's recess, was found to be infiltrating the base of the skull. The cytologic finding was correct, and possibly if it had been heeded in time radiation therapy might have been successfully instituted.

It is a paradoxical fact that, although squamous carcinoma is more prevalent in the uterus than in the tongue, the cure rate is much higher for uterine cancer than for lingual cancer. This would seem strange, since the upper vaginal vault is certainly less accessible than the oral cavity. Uterine cancer has a higher cure rate because it is discovered early mainly during routine cytologic examination. As a result of intense educational compaigns, both patients and physicians have learned the value of the routine application of this test.

Oral cancer is usually painless in its incipiency. Unless it develops in an easily viewed area, it is likely to go unnoticed, chiefly because of faulty oral examination procedures. Education in correct oral examination and popularization of the cytologic investigation will go a long way toward the early discovery of oral cancer.

Section by the

ARMED FORCES AND PUBLIC HEALTH SERVICE

GLUCOSE CONCENTRATIONS IN PAROTID FLUID AND BLOOD SERUM FOLLOWING INTRAVENOUS GLUCOSE LOADING

Ira L. Shannon, Major, USAF (DC), John R. Prigmore, Captain, USAF (MSC), and Robert A. Brooks, Captain, USAF (MC)

THE question of whether or not glucose is present in saliva has long been a point of research controversy. Our interest in this particular question was twofold; we were concerned with (1) the obvious implications of the presence of varying amounts of glucose in saliva in relation to present-day concepts of caries etiology and (2) the need for a clearer understanding of the seemingly very specific characteristics of glandular permeability to glucose. Although attempts have been made to measure human salivary glucose by older and less sensitive methods that were not specific for this variable, we know of no studies carried out on this fluid with specific enzyme and/or automatic dialysis methods. It was our purpose in the present study to ascertain the presence or absence of glucose in human parotid fluid by sampling specimens from fasting subjects and by carrying out conventional intravenous glucose-tolerance tests in blood serum and parotid fluid.

MATERIALS AND METHODS

Eight fasting male subjects between the ages of 17 and 22 years, each physically qualified for military service, served as subjects. Each was given 50 ml. of a 50 per cent aqueous glucose solution intravenously over a two- to three-minute period. Blood was withdrawn prior to the injection and ten, thirty, sixty, and 120 minutes after completion of the injection. Following a ten-minute accommodation period, a ten-minute parotid fluid sample was collected under gum base* (sugar-free) stimulation prior to glucose administration, and continuous stimulation provided a series of six ten-minute postglucose samples.

From the School of Aviation Medicine, Brooks Air Force Base, Texas.
*American Chicle Company.

Later parotid fluid samples were collected 120 and 180 minutes after glucose administration. All samples were analyzed for glucose by an automated ferricyanide method[1] and by the glucose oxidase procedure.[2]

RESULTS AND DISCUSSION

The mean values for all glucose determinations are shown in Table I. The finding that glucose levels were considerably higher with the ferricyanide method than with the enzyme procedure is in accord with the literature.[3, 4] Of primary interest is the identification of the additive ferricyanide-reducing substance(s) present in parotid fluid. When parotid fluid samples are treated with trichloroacetic acid and then dialyzed automatically, the ferricyanide method gives lower results that more nearly agree with those that follow the enzyme procedure. Thus, it seems possible that this additive substance is the same interfering substance that produces turbidity with molybdate, even after dialysis, in inorganic phosphate determinations.[1] Regardless of the type of chemical determination employed, the glucose concentration pattern of parotid fluid paralleled that of the blood serum, these responses being similar in nature to our previous parotid fluid adrenocortical steroid findings.[5, 6] We have now analyzed 140 fasting parotid fluid specimens by both these methods, and, without fail, we have found a measurable level of glucose. Although it is clear that the automated method is measuring reducing substance other than true glucose, either of these methods may be used in intravenous glucose-tolerance work, since the gross responses are the same. If the findings of the present study are verified in diabetic patients, parotid fluid must then be seriously considered for routine use in the clinical laboratory in carbohydrate metabolism evaluations.

TABLE I. COMPARISON OF AUTOMATIC FERRICYANIDE AND ENZYME METHODS FOR GLUCOSE DETERMINATION IN SERUM AND PAROTID FLUID

MINUTES AFTER INTRAVENOUS GLUCOSE	GLUCOSE (MG. PER CENT)			
	SERUM		PAROTID FLUID	
	AUTOANALYZER	GLUCOSE OXIDASE	AUTOANALYZER	GLUCOSE OXIDASE
0	82.9	68.5	1.03	.60
10	188.0	159.9	2.06	1.15
20			1.81	.78
30	103.0	83.7	1.09	.43
40			1.06	.40
50			1.05	.40
60	86.0	66.3	1.05	.42
120	95.4	75.5	1.05	.41
180			1.04	.50

SUMMARY

Glucose oxidase and automated ferricyanide procedures carried out on healthy young men indicated the following:

1. There is a measurable level of glucose in human fasting parotid saliva.

2. This parotid-fluid glucose concentration is sensitive to the administration of intravenous glucose and closely parallels the serum level.

The authors express appreciation to J. F. McAnear, E. D. Dinger, L. Crawford, and D. Weiss for their technical assistance.

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PAROTID GLAND FLOW RATE AND PAROTID FLUID UREA CONCENTRATION

Ira L. Shannon, Major, USAF (DC), and*
*John R. Prigmore, Captain, USAF (MSC)***

UREA is an extremely diffusible compound that serves as an excellent tool in cellular permeability studies. Human and animal experimentation concerned with urea dosage and subsequent urea determinations in blood, urine, tissues, and parotid fluid are being carried out in these laboratories in an effort to gain insight into the intimate mechanisms of specificity of function of the parotid gland. Basic to the understanding of results of studies of this type is a thorough understanding of the relationship of parotid gland flow rate and the urea concentration of parotid fluid. It was the purpose of the present study to ascertain the flow rate–urea concentration relationships in human subjects under conditions of greatly varying stimulation and to determine the response of these two variables to prolonged stimulation.

Previous studies of the effect of parotid gland flow rate on urea concentration have not led to uniform conclusions. Albrectsen and Thaysen[1] collected parotid saliva under "resting conditions," with lemon-flavored candies as the eliciting agent, and with subcutaneous injections of 5 to 15 mg. of pilocarpine hydrochloride in isotonic saline. They found that the concentration of urea in their samples varied with the rate of salivary secretion. The salivary plasma-urea ratio was independent of flow rate at rates of flow greater than 0.5 ml. per minute, but at lower flow rates the ratio gradually rose with decreases in flow rate. Barnett and Bramkamp[2] analyzed parotid fluid collected from eighteen subjects with differing concentrations (0.05 and 0.5 per cent) of tartaric acid. The weaker acid gave a flow rate of 0.31 ml. per minute, while the 0.5 per cent solution produced 1.39 ml. per minute. The urea concentration findings of 29.3 and 22.1 mg. per cent, respectively, point out the negative correlation with rate of flow. In a later study, Bramkamp[3a] gave his subjects oral doses of 1/5 gr. of atropine sulfate or 1/16 gr. pilocarpine hydrochloride and, one

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The opinions herein expressed are those of the authors and should not be construed as representing official Air Force policy.

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hour later, collected parotid fluid samples under paraffin or lemon stimulation. He found that neither the drugs nor the rate of secretion caused any appreciable change in the urea concentration of parotid fluid.

PROCEDURE

Three separate experiments were carried out to determine the relationship between parotid gland flow rate and the urea concentration of the resulting parotid fluid. Different subjects (all healthy young men) and different stimulation patterns were employed in each of these studies. A fourth experiment, three hours in duration, was designed to ascertain fatigue characteristics of the parotid gland as they pertain to rate of flow and to urea secretion.

All test specimens were preceded by an accommodation (waste) sample collected under identical conditions. Volume was read directly from the graduated centrifuge tubes used as collection vessels. Urea nitrogen was determined by the diacetyl monoxime method[4-6] as adapted to parotid fluid analysis[7] on the Autoanalyzer.* The different procedural details of each experiment are detailed separately along with the results of the individual studies.

In the first three experiments, correlation coefficients between flow rate and urea concentration were computed for each pair of observations for each subject. An average "within-subjects" coefficient was then calculated. Also, subject means for each of the observations for each variable were computed and a "between-subjects" correlation coefficient was calculated. The probabilities of significance for all coefficients were determined.

RESULTS AND DISCUSSION

Experiment 1.—Each of fourteen subjects was given 16 mg. of pilocarpine hydrochloride by mouth and, after initiation of flow, a series of fifteen five-minute parotid fluid samples were collected from each subject. Means and

TABLE I. MEANS AND STANDARD DEVIATIONS FOR FLOW RATE AND UREA CONCENTRATION OF PAROTID FLUID

FIVE-MINUTE SAMPLE NO.	FLOW RATE (ML./MIN.)		UREA (MG. PER CENT)	
	MEAN	S.D.	MEAN	S.D.
1	0.616	0.321	26.86	8.91
2	0.743	0.291	22.29	4.41
3	0.823	0.414	21.03	3.48
4	0.900	0.523	21.77	3.51
5	0.910	0.495	20.92	2.47
6	0.999	0.633	20.52	2.83
7	1.029	0.727	21.14	3.62
8	1.020	0.696	21.13	3.88
9	0.874	0.418	21.34	3.57
10	0.793	0.414	21.75	3.72
11	0.747	0.346	22.09	3.85
12	0.660	0.360	23.63	4.46
13	0.590	0.291	24.16	4.45
14	0.537	0.279	24.86	3.93
15	0.481	0.278	26.22	4.47

Fourteen subjects received 16 mg. pilocarpine orally. The correlation coefficient was -0.83 ($P < .01$).

* Technicon Instruments Corporation, Chauncey, New York.

standard deviations for flow rate and urea concentration are shown in Table I, and the means are plotted in Fig. 1. The correlations between flow rate and urea concentration did not differ significantly between subjects. The average "within-subjects" correlation was –0.83 ($P < .01$). The "between-subjects" correlation coefficient was not significant.

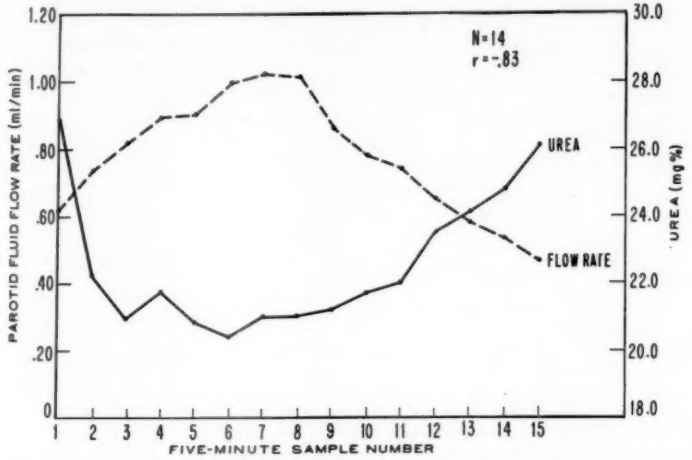

Fig. 1.—Means for parotid fluid flow rate and urea following 16 mg. pilocarpine hydrochloride orally.

Experiment 2.—A series of fifteen five-minute test specimens were collected from fifteen subjects under varying conditions of exogenous stimulation. Samples 1 and 2 were elicited with one-half stick of gum base; specimens 3 to 6 were collected as the subjects chewed one and one-third sticks of sugared gum, the bolus being replaced every five minutes; specimens 7 to 12 were five-minute

TABLE II. MEANS AND STANDARD DEVIATIONS FOR FLOW RATE AND UREA CONCENTRATION OF PAROTID FLUID ELICITED BY DIFFERENT EXOGENOUS STIMULI (FIFTEEN SUBJECTS)

FIVE-MINUTE SAMPLE NO.	EXOGENOUS STIMULANT	FLOW RATE (ML./MIN.)		UREA (MG. PER CENT)	
		MEAN	S.D.	MEAN	S.D.
1	Gum base	0.397	0.197	26.02	4.59
2	Gum base	0.383	0.168	26.58	5.26
3	Sugared gum	1.053	0.343	22.02	2.85
4	changed every five	0.961	0.267	21.22	2.87
5	minutes (Nos. 3-6)	0.991	0.232	21.55	2.71
6		0.984	0.218	21.71	3.04
7	Bolus No. 6 left	0.736	0.257	22.45	2.88
8	in the mouth	0.573	0.176	23.36	3.09
9	unchanged	0.532	0.170	24.20	3.55
10	(Nos. 7-12)	0.528	0.188	24.81	3.92
11		0.467	0.128	25.01	4.15
12		0.461	0.156	25.12	3.81
13	Sugared gum	1.140	0.335	22.15	2.73
14	changed every	1.035	0.282	21.74	2.79
15	five minutes	1.040	0.276	21.84	2.45

samples collected with bolus 6 left in the mouth and not renewed; and samples 13 to 15 were obtained with one and one-third sticks of sugared gum, the bolus being changed every five minutes. Means and standard deviations for flow rate and urea concentration for the individual samples are shown in Table II and

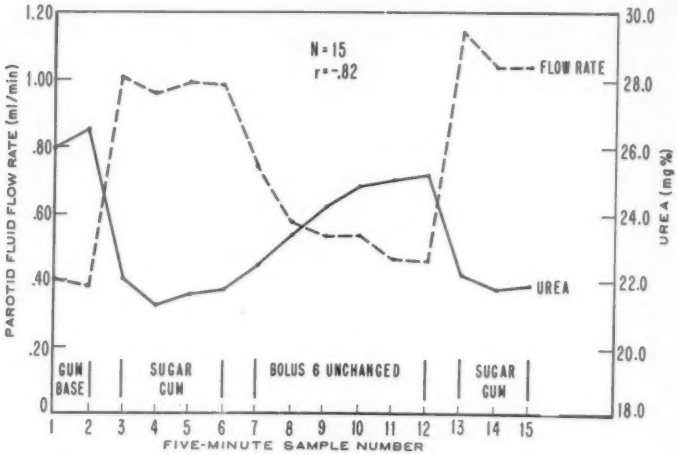

Fig. 2.—The effect of varying flow rates on urea concentration.

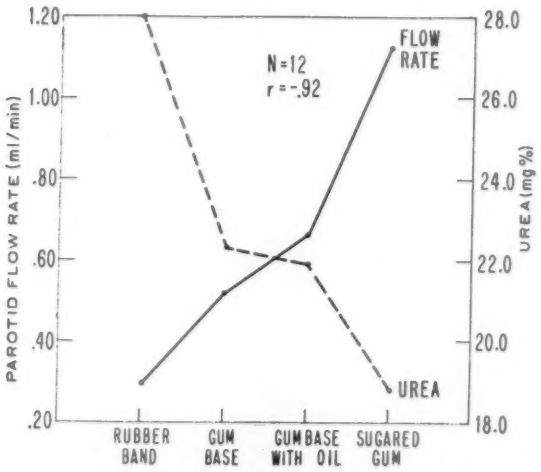

Fig. 3.—Parotid fluid flow rate and urea interrelations.

the means are graphed in Fig. 2. When samples 1 and 2 (gum base) were combined for all subjects, a flow rate mean of 0.390 ml. per minute (S.D., 0.179) and a urea mean of 26.31 mg. per cent (S.D., 4.87) resulted. Samples 3 through 6 (sugared gum, renewed) provided a flow rate mean of 1.000 ml. per minute

(S.D., 0.239) and a urea mean of 21.65 mg. per cent (S.D., 2.75); specimens 7 to 12 (bolus 6, not renewed) gave a flow rate mean of 0.550 ml. per minute (S.D., 0.169) and a urea mean of 24.16 mg. per cent (S.D., 3.53); samples 13 to 15 (sugared gum, renewed) provided a flow rate mean of 1.072 ml. per minute (S.D., 0.288) and a urea mean of 21.91 mg. per cent (S.D., 2.59). The average "within-subjects" correlation coefficient was –0.82. These correlations were significantly different from one subject to another. The "between-subjects" correlation, computed from the subject means, was –0.01 (N.S.).

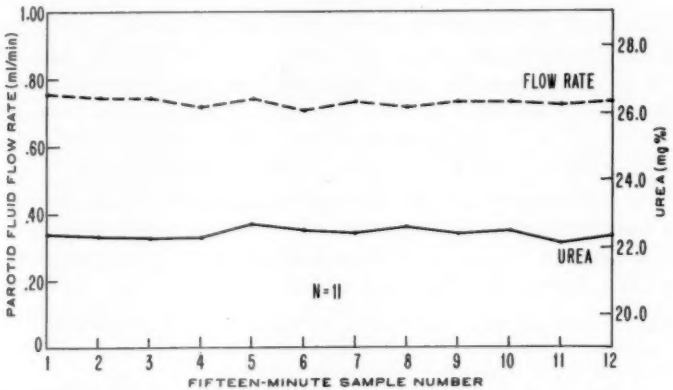

Fig. 4.—Effect of prolonged stimulation on flow rate and urea concentration.

Experiment 3.—Flow rate and urea concentration were measured four times, under different stimulus conditions, in each of twelve subjects. Consecutive five-minute test samples were collected under the stimulus of one rubber band, gum base, gum base with oil, and sugared gum. A five-minute accommodation (waste) sample was collected with each agent prior to its use in collecting the test specimen. The flow rate mean increased from 0.300 (S.D., 0.114) to 0.517 (S.D., 0.279) to 0.662 (S.D., 0.454) to 1.072 (S.D., 0.288) ml. per minute as stimulus intensity was increased. Concurrently, corresponding urea levels shifted from 27.97 (S.D., 14.69) to 22.33 (S.D., 5.44) to 21.88 (S.D., 5.34) to 18.77 (S.D., 5.01) mg. per cent. These means are plotted in Fig. 3. The correlations, calculated for each subject, did not differ significantly. The average "within-subjects" correlation was –0.92 ($P < .01$), while the "between-subjects" correlation was found to be 0.42 ($P < .05$). This "between-subjects" significance is due primarily to the extraordinarily high flow rate and urea values for one subject. The "between-subjects" rank correlation coefficient for this experiment was only 0.07.

Experiment 4.—In this experiment a series of twelve fifteen-minute parotid fluid samples were collected from each of eleven subjects under the stimulation of sugared gum, one and one-third sticks, renewed every five minutes. Flow rate and urea concentration were determined on each of the samples over the

three-hour period in an effort to ascertain whether or not there was a change in either of these variables with time, that is, whether or not there was glandular fatigue in these respects. The effect of time on both volume and urea levels was determined and found not to be significant; over the three-hour period there was no gland fatigue for either of the variables under study. The volume means varied from 0.706 to 0.753 ml. per minute, while the urea mean range was from 22.1 to 22.7 mg. per cent. These means are shown in Fig. 4.

SUMMARY

In a series of three experiments the relationship between parotid gland flow rate and parotid fluid urea concentration was determined. In each instance a significant ($P < .01$) negative correlation was found between these two variables. The data were all combined and an average "within-subjects" correlation coefficient of –0.83 ($P < .001$) was calculated. The average "between-subjects" correlation coefficient of 0.05 was not significantly different from zero.

In a fourth experiment parotid flow was elicited continuously for three hours in eleven subjects. The effect of time on flow rate and urea concentration was insignificant, that is, there was no apparent gland fatigue effect on either variable during the three-hour period.

The authors express their appreciation to Richard McNee and Albert Rahe for the statistical analysis and to medical technicians J. F. McAnear, E. D. Dinger, L. Crawford, Dorothy Weise, and Eli Espinosa for technical assistance.

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ANNOUNCEMENTS

American Society of Dentistry for Children

Do you treat children in your practice? If you do, the American Society of Dentistry for Children can help you enjoy your young patients. Join the Society now and benefit immediately by attending the national meeting which will be held at the Ambassador Hotel in Los Angeles, California, Oct. 14 to 16, 1960, immediately preceding the American Dental Association's meeting.

Make application to National Office, American Society of Dentistry for Children, c/o Dr. C. F. Tuma, 13201 Miles Ave., Cleveland 5, Ohio, or Dr. Carl G. Cohen, Secretary, ASDC, 84 Leonard St., Belmont Center 78, Massachusetts.

University of Alabama

The School of Dentistry will offer two refresher courses during October, 1960:

Oral Rehabilitation. Oct. 22 and 23, 1960. Jerome M. Schweitzer, D.D.S.
Hospital Protocol and Dental Therapeutics. Oct. 29 and 30, 1960. Charles McCallum, D.M.D., M.D.

Further information may be obtained from the Director, Refresher Course Program, University of Alabama School of Dentistry, 1919 7th Ave. South, Birmingham, Alabama.

Boston University

The Division of Graduate Studies of the Department of Stomatology announces that a graduate course in orthodontics will begin in September, 1960, under the direction of Dr. Herbert I. Margolis. Further information may be obtained by writing to Boston University School of Medicine, Department of Stomatology, 80 East Concord St., Boston, Massachusetts.

American Association of Endodontists

The American Association of Endodontists will sponsor a symposium entitled "Biology of Dental Pulp" on Thursday, Feb. 2, 1961, at the Conrad Hilton Hotel in Chicago, Illinois. The program will be open to members and nonmembers alike. The fee for the entire day, including lunch with the clinicians, is $25.00. Checks, made payable to the Association, should be forwarded to Dr. L. Parris, 1930 Chestnut St., Philadelphia, Pennsylvania. Attendance is limited.

Mid-Continent Dental Congress

The 1960 Mid-Continent Dental Congress, sponsored by the St. Louis Dental Society, will be held at the Chase Hotel in St. Louis, Missouri, Nov. 27 to 30, 1960. The schedule is as follows:

Sunday, November 27

Special four-hour course: "Practice Administration—Improve Dentistry Faster Without Increased Cost to the Patient." John L. Woehler, D.D.S., Sierra Madre, California.

Monday, November 28

Oral Rehabilitation. Ted Gordon, D.D.S., Chicago, Illinois.

Clinical Features and Recognition of Common Lesions of the Oral Mucosa. Lester W. Burket, D.D.S., M.D., Philadelphia, Pennsylvania.

Newer Concepts in Endodontics. George C. Stewart, D.D.S., Philadelphia, Pennsylvania.

Tuesday, November 29

Normal Functional Occlusion. Angelo D'Amico, D.D.S., Stockton, California.

Making Dentistry for Children Pleasurable and Profitable. Clinton C. Emmerson, D.D.S., Los Angeles, California.

What Place Has Periodontics in General Practice of Dentistry? Frank E. Beube, D.D.S., New York, New York.

Evaluation of Newer Dental Materials and Factors Affecting Their Clinical Success. Ralph W. Phillips, Indianapolis, Indiana.

Techniques for Positive Healing After Surgery. John C. Versnel, D.D.S., St. Louis, Missouri.

Wednesday, November 30

Complete Dentures. Vincent R. Trapozzano, D.D.S., St. Petersburg, Florida.

Additional information may be obtained from the St. Louis Dental Society, 8013 Maryland Ave., St. Louis 5, Missouri.

Southern California Academy of Endodontists

An all-day scientific meeting will be held at the Beverly Hills Hotel in Beverly Hills, California, on Saturday, Oct. 15, 1960, preceding the 1960 meeting of the American Dental Association. The meeting will feature a nationally recognized guest speaker, table clinics, and a seminar luncheon. All members of the American Dental Association are invited to attend.

There will be a registration fee of $10.00 (including lunch). Checks should be mailed to Dr. Sanford Golden, Program Chairman, 1001 Gayley, Los Angeles 24, California.

Southern California Academy of Oral Pathology

The Academy will be host for a meeting on oral pathology at the Beverly Hilton Hotel in Los Angeles, California, on Oct. 16, 1960, the day preceding the opening of the American Dental Association meeting. Two outstanding oral pathologists—George Greene and Robert Gorlin—will be the featured essayists. All members of the American Academy of Oral Pathology and of organizations affiliated with ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY are cordially invited to attend.

Reservations and a check for $6.50 may be sent to the secretary, Dr. Arthur Barrett, 22030 Sherman Way, Canoga Park, California.

Army Graduate School of Dentistry

The Army Graduate School of Dentistry, Walter Reed Army Institute of Research, Washington, D. C., announces the following postgraduate dental professional short courses:

Prosthodontics. Nov. 28 to Dec. 2, 1960.

Oral Surgery. Jan. 9 to 13, 1961.

Oral Diagnosis and Therapeutics. May 15 to 19, 1961.

Preventive Dentistry. June 5 to 9, 1961.

Attendance is open to (1) dental corps officers of the Armed Forces on active duty, (2) dental corps officers of the Armed Forces not on active duty, and (3) civilian dentists from other health agencies and communities near Walter Reed Army Institute of Research.

Boston University School of Medicine

The Department of Stomatology, Division of Graduate Studies, Boston University School of Medicine and the Massachusetts Memorial Hospitals, announces the following postgraduate courses:

Occlusal Adjustment. Bernard S. Chaikin, Henry M. Goldman, Gerald M. Kramer, William Pendergast, Jack Bloom, and associates. Sept. 12 to 16, 1960. $200.00.

Enodontics. Herbert Schilder. Sept. 12 to 16, 1960. $175.00.

Periodontal Therapy. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, Jack Bloom, and associates. Nov. 7 to 11, 1960. $175.00.

Fixed Bridge Prosthesis. Leo Talkov, David J. Baraban, and Lloyd Warshauer. Nov. 14 to 18, 1960. $175.00.

Full Denture Prosthesis. Chester Landy. Dec. 12 to 16, 1960. $150.00.

For further information about specific postgraduate courses and for application blank, write to Director of Postgraduate Courses, Department of Stomatology, Massachusetts Memorial Hospitals, 750 Harrison Ave., Boston 18, Massachusetts.

Tufts University

Tufts University School of Dental Medicine will offer a special participation course in periodontology (DPG 605) Oct. 31 to Nov. 4, 1960. The course will be under the direction of Dr. Irving Glickman and staff. Tuition will be $175.00.

Emphasis will be placed on learning by clinical experience. The "bone factor" concept for the diagnosis, determination of prognosis, and treatment planning for individual teeth and for the dentition as a functioning unit will be explained in detail.

Further information may be obtained from the Director of the Division of Graduate and Postgraduate Studies, Tufts University School of Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

REVIEWS OF THE LITERATURE

BOOK REVIEW

Die Neuzeitliche Kieferorthopädische Praxis. H. Stockfisch. Second edition. Heidelberg, Germany, 1959, Dr. Alfred Hüthig Verlag, G. M. B. H., 455 pages, 1,115 illustrations. Price, DM48-.

The first edition of this book was published in 1956. The second edition has been revised and enlarged. The book contains 154 pages dealing with diagnosis and description of the various systems of treatment. The rest of the book is taken up with therapy by means of activators and prosthetic plates. Many interesting new appliances are described, and their practical application is excellently illustrated. The book contains 2½ pages of bibliography, mostly the works of German authors.

K. H. I.

ABSTRACTS OF CURRENT LITERATURE

Bacterial Invasion of Blood After Oral Surgical Procedures. Alexander Schirger, M.D., William J. Martin, M.D., R. Quentin Royer, D.D.S., and Gerald M. Needham, PH.D. J. Lab. & Clin. Med. **55**: 376-380, March, 1960.

In 27 of 50 patients who had not received an antibiotic, cultures of blood drawn immediately after oral surgical procedures yielded bacteria. Ten of these positive cultures grew streptococci of the mitis group, and one yielded *Staphylococcus aureus.* In eight of a similar group of fifty patients who had received phenoxymethyl penicillin preoperatively every six hours for four doses, totaling 4,000,000 U., cultures of blood drawn immediately after surgery grew bacteria; however, no streptococci of the mitis group were encountered. When half this dose, or 2,000,000 U., was used in twenty-seven patients, cultures of blood from five immediately after surgery grew bacteria; the blood of one of these five yielded *Streptococcus mitis.*

Phenoxymethyl penicillin is effective in decreasing the incidence of bacterial invasion of the blood after oral surgery. When given in doses employed in this study, the agent seems to minimize invasion of the blood by streptococci of the mitis group. A total of 4,000,000 U. given preoperatively in four equally divided doses proved as effective as have other forms of penicillin given on differing schedules by other investigators.